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Assessment and Management of Pharmaceuticals and Personal Care Products in the Canadian Environment: Proceedings of a Multi-Stakeholder Workshop

Évaluation et gestion des produits pharmaceutiques et des produits d'hygiène et de beauté dans l'environnement canadien : compte rendu d'un atelier à intervenants multiples

Hosted by / Organisé par
Environment Canada and Health Canada
Environnement Canada et Santé Canada

Queen's Landing Inn, Niagara-on-the-Lake
February 24 –27, 2002
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Executive Summary

Recent studies in Europe and the United States have documented the presence of a wide variety of substances contained in pharmaceuticals and personal care products (PPCPs) in the environment. Municipal sewage, agricultural and aquaculture wastes have been identified as sources of PPCPs such as antibiotics, blood lipid regulators, analgesics, anti-inflammatories, anti-epileptics, natural and synthetic hormones, fragrances (musks), nonylphenol ethoxylates, disinfectants and anti-parasiticides. Many of these substances are designed to target specific biological functions at therapeutic doses. There is mounting evidence that some of these chemicals have the potential to induce adverse health effects in non-target species and possibly humans when exposed to low levels. Effects of concern include disruption of development and reproduction in exposed individuals and their offspring, as well as the enhancement of antibiotic resistant bacteria. There is great uncertainty what the potential long-term human health and ecological health consequences may be resulting from continuous low-level exposure to these substances, especially in sensitive life stages and populations. Release of PPCPs into the environment will continue, and will diversify with new product developments dependent upon changing use patterns in humans and animal production. New PPCPs, especially drugs, are likely to be engineered to be increasingly persistent in the body, specific and biologically active.

Few data are available to characterize the sources, exposure and effects of PPCPs in the Canadian environment. In recognition of the importance of the issue and the federal mandate to protect the health of Canadians and the environment, a scientific workshop entitled *Assessment and Management of Pharmaceuticals and Personal Care Products in the Canadian Environment* was held February 24 to 27, 2002, in Niagara-on-the–Lake, Ontario. This multi-stakeholder workshop sponsored by Health Canada and Environment Canada provided a forum to discuss PPCPs within a Canadian and international perspective. The main objective of the workshop was to identify major research and risk management needs in Canada. To provide an international multidisciplinary perspective, presentations were made by scientists and regulators from the EU, US and Canada. Invited participants representing industry, government, academia and public interest groups provided a broad spectrum of expertise and perspectives. Informal breakout and round table sessions were designed to promote discussion, identify and prioritize research needs.

The proceedings of the workshop are to be published as a government report as well as in the peer reviewed literature to maximize the distribution of the information. The major conclusions and recommendations from the workshop as well as a tabulated summary of research priorities identified by workshop participants are presented here.

Major Conclusions of the Scientific Workshop

There is a need:

- to clearly define the scope of the issue within a Canadian context,
- to immediately obtain scientific data on exposure and effects of PPCPs in the Canadian environment,
- to collaborate internationally across sectors to address knowledge gaps and reduce scientific uncertainty,
- for an interdisciplinary, multi-sector approach to support development of a Canadian regulatory framework in harmonization with international organizations (e.g. VICH, OECD),
- to implement a comprehensive national science program to address risk assessment and risk management of PPCPs in the Canadian environment,
- for the development and implementation of "best management practices" and risk management options,
- for a national communication strategy.

Recommendations for the Implementation of a National Science Agenda

- Create a multidisciplinary research initiative in cooperation with all levels of government, industry and academia.
- Prioritize concerns by reviewing existing information to identify sources, distribution, and use patterns of PPCPs, their likely environmental fate, potency, mechanism of action, and assessment methods.
- Design and implement a data collection program for assessing exposure to PPCPs in Canada (wastewater, drinking water, groundwater, surface water and agricultural soils).
- Establish a network within the international scientific community to promote the exchange of scientific information to minimize duplication of effort and capitalize on existing expertise and programs.
- Contribute to the international programs for test development and validation and integrate international standardized tests within the Canadian regulatory framework.
- Engage other levels of government to address agricultural practices, wastewater technology, and drinking water quality across the nation.
- Implement a risk communication strategy to educate industry, government and public stakeholders on appropriate use, disposal and management practices for PPCPs.

Table 1. Research priorities identified during a multi-stakeholder workshop, "Assessment and Management of Pharmaceuticals and Personal Care Products in the Canadian Environment", Niagara-on-the-Lake, Ontario, Feb. 24-27, 2002.

	Research Priorities for Pharmaceuticals and Personal Care Products (PPCPs)
1.	Devising methods and technologies for treating wastes (municipal, agricultural) to reduce the release of PPCPs.
2.	Evaluating human exposure from drinking water (sensitive groups, the elderly, children, etc.).
3.	Developing environmental effects assays (acute, chronic, life-cycle) at appropriate trophic levels.
4.	Developing best management practices for land application of animal and municipal wastes.
5.	Developing chemical and biological analytical methods for assessing exposure of PPCPs.
6.	Developing practices to reduce the use of PPCPs of concern (e.g. best management practices).
7.	Developing models to predict loading, fate and exposure.
8.	Evaluating environmental exposure from wastewater (e.g. Sewage Treatment Plants).
9.	Assessment of environmental effects including baseline studies (e.g. Environmental Effects Monitoring Program approach).
10.	Prioritization of PPCPs of concern (volumes, loadings, pathways, bioaccumulation).
11.	Better understanding of effects of mixtures (e.g. STP whole effluents, Toxicity Identification Evaluation approach).
12.	Development and validation of appropriate methods for assessing effects of PPCPs (harmonization with OECD, US-EPA test development).
13.	Improved fundamental understanding of mode of action and pharmacokinetics of PPCPs in humans and non-target species.
14.	Evaluating environmental antimicrobial resistance and response to PPCPs.
15.	Evaluating and developing human health effects assays (high dose vs. low dose).
16.	Human disease and human health surveillance (e.g. antimicrobial resistance, neurological and behavioral development).
17.	Evaluating environmental exposure from agriculture (e.g. manure, biosolids application).
18.	Developing and validating predictive tools (e.g. models, Quantitative Structure Activity Relationships).
19.	Determine relevance of current assessment methods.
20.	Evaluating environmental exposure from aquaculture.

Each participant was given the opportunity to rank the priorities by voting.

Sommaire à l'intention de la Direction

Des études récentes en Europe et aux États-Unis font état de la présence dans l'environnement d'une vaste gamme de substances provenant de produits pharmaceutiques et de produits d'hygiène et de beauté (PPHB). Les eaux usées des municipalités ainsi que les déchets provenant de l'agriculture et de l'aquaculture ont été identifiées comme sources de PPHB. Parmi ces derniers, on peut mentionner les suivants : antibiotiques, régulateurs des lipides plasmatiques, analgésiques, anti-inflammatoires, antiépiléptiques, hormones naturelles et synthétiques, parfums (muscs), éthoxylates de nonylphénol, désinfectants et antiparasiticides. Beaucoup de ces substances sont conçues pour cibler, à dose thérapeutique, des fonctions biologiques spécifiques. Il y a de plus en plus de faits qui montrent que ces produits chimiques ont le pouvoir d'exercer des effets toxiques sur la santé d'espèces non visées et peut-être même sur la santé humaine, lorsqu'il y a exposition à de faibles concentrations. Parmi les effets préoccupants, il y a les troubles au niveau du développement et de la reproduction chez les individus exposés et leur descendance, ainsi que le renforcement des bactéries résistant aux antibiotiques. Il existe une grande incertitude quant aux conséquences à long terme sur la santé humaine et la santé environnementale d'une exposition continue à de faibles concentrations de ces substances, particulièrement chez les segments sensibles de la population et aux stades critiques de la vie. Les rejets de PPHB dans l'environnement vont se poursuivre et se diversifier avec le développement de nouveaux produits au gré de l'évolution de la consommation dans la population et dans le secteur de la production animale. On peut s'attendre à ce que des PPHB, et particulièrement des médicaments, soient mis au point pour être de plus en plus persistants dans l'organisme, avoir une action spécifique et être biologiquement actif.

Pour les PPHB, on ne possède que peu de données permettant de caractériser les sources, l'exposition et les effets dans l'environnement canadien. Vu l'importance de la question et le mandat du gouvernement fédéral de protéger la santé des Canadiens et de leur environnement, un atelier scientifique, intitulé *Évaluation et gestion des produits pharmaceutiques et des produits d'hygiène et de beauté dans l'environnement canadien*, a été organisé du 24 au 27 février 2002 à Niagara-on-the–Lake (Ontario). Cet atelier à intervenants multiples, parrainé par Santé Canada et Environnement Canada, représentait une tribune pour discuter des PPHB dans une perspective tant canadienne qu'internationale. Le principal objectif de l'atelier était de caractériser les principaux besoins en recherche et en gestion du risque au Canada. Pour avoir un point de vue international et multidisciplinaire, on a invité des scientifiques et des responsables en réglementation de l'UE, des États-Unis et du Canada à faire des présentations. Les participants invités, issus des secteurs industriels, gouvernementaux et universitaires ainsi que des groupes de défense de l'intérêt public, présentaient un vaste champ d'expertise et de perspectives. Des réunions informelles en petits groupes et des tables rondes étaient prévues pour faciliter la discussion et identifier ou prioriser les besoins en recherche.

Le compte rendu de l'atelier sera publié en tant que rapport gouvernemental ainsi que dans des publications spécialisées pour maximiser la diffusion de l'information. On présente ici les principales conclusions et recommandations de l'atelier, ainsi qu'un

résumé, sous forme de tableau, des priorités en recherche déterminées par les participants à l'atelier.

Principales conclusions de l'atelier scientifique

Il faut :

- définir clairement la portée de la question dans un contexte canadien,
- obtenir immédiatement des données scientifiques sur l'exposition aux produits pharmaceutiques et de soins personnels (PPSP) dans l'environnement au Canada,
- collaborer avec les chercheurs de multiples secteurs à l'échelle internationale pour combler les lacunes dans les connaissances et réduire l'incertitude scientifique,
- adopter une approche interdisciplinaire et multisectorielle afin d'appuyer l'établissement d'un cadre réglementaire au Canada et l'harmoniser avec ceux d'organisations internationales (p. ex. VICH, OCDE),
- mettre en oeuvre un programme scientifique national complet visant l'évaluation et la gestion des risques liés aux PPSP dans l'environnement au Canada,
- élaborer et mettre en oeuvre des « pratiques exemplaires de gestion » et des options de gestion des risques,
- adopter une stratégie de communication nationale.

Recommandations pour la mise en oeuvre d'un programme scientifique national

- Mettre sur pied une initiative de recherche multidisciplinaire en coopération avec tous les paliers de gouvernement, l'industrie et le milieu universitaire.
- Déterminer les enjeux prioritaires en examinant les données existantes afin de déterminer les sources, la répartition et les profils d'utilisation des PPSP, leur devenir probable dans l'environnement, leur activité, leur mécanisme d'action et des méthodes d'évaluation.
- Élaborer et mettre en oeuvre un programme de collecte de données afin d'évaluer l'exposition aux PPSP au Canada (eaux usées, eau potable, eaux souterraines, eaux de surface et champs cultivés).
- Établir un réseau de chercheurs au sein de la communauté scientifique internationale afin de promouvoir l'échange de renseignements scientifiques de façon à réduire au minimum le dédoublement des efforts et de miser le plus possible sur l'expertise et les programmes existants.
- Contribuer aux programmes internationaux en vue de mettre au point et de valider des tests, et intégrer les tests normalisés à l'échelle internationale dans le cadre réglementaire canadien.
- Obtenir l'engagement d'autres paliers de gouvernement afin de gérer les questions liées aux pratiques agricoles, aux technologies concernant les eaux usées et à la qualité de l'eau potable partout au pays.

- Mettre en oeuvre une stratégie de communication des risques afin de sensibiliser les intervenants de l'industrie et du gouvernement ainsi que la population aux utilisations et aux méthodes d'élimination et de gestion appropriées des PPSP.

Tableau 1. Priorités de recherche établies au cours de l'atelier multipartite « Évaluation et gestion des produits pharmaceutiques et de soins personnels dans l'environnement au Canada », tenu à Niagara-on-the-Lake (Ontario) du 24 au 27 février 2002

	Priorités de recherche relatives aux produits pharmaceutiques et de soins personnels (PPSP)
1.	Concevoir des méthodes et des technologies de traitement des déchets (municipaux, agricoles) afin de réduire le rejet des PPSP.
2.	Évaluer l'exposition des humains via l'eau potable (groupes vulnérables, personnes âgées, enfants, etc.).
3.	Mettre au point des épreuves permettant d'évaluer les effets environnementaux (aigus, chroniques, cycle de vie) aux niveaux trophiques appropriés.
4.	Mettre au point des pratiques exemplaires de gestion de l'épandage de déchets d'origine animale et d'eaux résiduaires urbaines sur les terres.
5.	Mettre au point des méthodes d'analyse chimique et biologique afin d'évaluer l'exposition aux PPSP.
6.	Établir des pratiques visant à réduire l'utilisation des PPSP qui sont préoccupants (p. ex. pratiques exemplaires de gestion).
7.	Élaborer des modèles permettant de prévoir les charges et le devenir de ces produits, ainsi que le degré d'exposition.
8.	Évaluer l'exposition de l'environnement aux eaux usées (p. ex. stations d'épuration des eaux usées).
9.	Évaluer les effets sur l'environnement, notamment par l'étude des conditions de base (p. ex. programme de suivi des effets sur l'environnement).
10.	Établir les priorités quant aux PPSP préoccupants (volumes, charges, voies d'introduction, bioaccumulation).
11.	Améliorer la compréhension des effets de mélanges (p. ex. effluent total des stations d'épuration d'eaux usées, approche d'évaluation des données sur la toxicité).
12.	Élaborer et valider les méthodes appropriées pour évaluer les effets des PPSP (harmonisation avec le processus de mise au point de tests de l'OCDE, de l'USEPA).

	Priorités de recherche relatives aux produits pharmaceutiques et de soins personnels (PPSP)
13.	Améliorer la compréhension fondamentale du mode d'action et de la pharmacocinétique des PPSP chez les humains et les espèces non ciblées.
14.	Évaluer la résistance aux antimicrobiens et la réaction de l'environnement à l'exposition aux PPSP.
15.	Évaluer et mettre au point des épreuves relatives aux effets sur la santé humaine (forte dose / faible dose).
16.	Assurer la surveillance des maladies et de la santé des humains (p. ex. résistance aux antimicrobiens, développement du système nerveux et du comportement).
17.	Évaluer l'exposition environnementale liée à l'agriculture (p. ex. épandage de fumier, de biosolides).
18.	Élaborer et valider des outils de prévision (p. ex. modèles, rapports constitution-activité quantitatifs).
19.	Déterminer la pertinence des méthodes d'évaluation actuelles.
20.	Évaluer l'exposition environnementale liée à l'aquaculture.

Chaque participant a été invité à voter pour indiquer ses priorités.

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The success of the workshop was dependent on the tireless support of many individuals in particular Jenn Dykeman, Rod McInnis and Kim Evraire. The support and advice of Jim Maguire and Linda Gysbers was greatly appreciated. Finally, thank you to the staff at the Queen's Landing, Niagara-on-the-Lake, for providing quality facilities and services throughout the workshop.

Many thanks go to the sponsors and contributors who made this workshop possible. Specifically, many of the participant's home organizations supported their time and travel expenses to participate in the workshop. Special recognition goes to the management of the National Water Research Institute, Environment Canada, the Toxic Pollution Prevention Directorate, Environment Canada, and the Office of Regulatory and International Affairs, Health Canada, for their strong support of this initiative and providing financial and infrastructure support to the workshop.

Workshop Sponsors

Office of Regulatory and International Affairs
Health Products and Food Branch
Health Canada

National Water Research Institute
Environmental Conservation Service
Environment Canada

Toxics Pollution Prevention Directorate
Environmental Protection Service
Environment Canada

Wastewater Technology Centre
Environmental Protection Service
Environment Canada

Introduction

Recent studies around the globe have detected a wide variety of pharmaceuticals and personal care products in the environment. Sewage may contain a vast array of pharmaceuticals such as antibiotics, blood lipid regulators, analgesics, anti-inflammatories, and beta-blockers, as well as cosmetics and related products such as fragrances (musks), skin care products, disinfectants and antiseptics. Current livestock and aquaculture production practices include the use of a wide variety of pharmaceuticals to enhance animal health and efficient food production including antimicrobials (antibiotics), growth enhancers, feed supplements and other medicinal products. The dominant routes of entry of these substances and their metabolites into the environment are therefore direct discharge of sewage treatment system effluents (municipal treatment plants, lagoons or septic beds), agricultural application of sewage sludges, and the agricultural management of animal wastes (manures). Although the exposure to the environment, and especially to humans, is expected to be low there are few data available for the Canadian environment.

Traditionally, pharmaceuticals and personal care products have not been viewed as environmental pollutants. However, the potential for these substances to cause a variety of physiological responses in non-target species, has raised concerns for possible impacts on the environment. Although, these substances are usually found in very low concentrations in the environment, continuous low dose exposure, especially to sensitive life stages, to these complex mixtures may have significant effects on individuals, populations or ecosystems. The ecological impact of long-term exposure to large mixtures of biologically active chemicals is also unknown. Many of these chemicals are very persistent in treatment systems and in the environment and are designed to target specific biological functions at very low doses. Chemicals found in sewage and manure, such as synthetic estrogens, are known to have biological consequences at extremely low exposures. Exposure of biota to even low doses during critical or sensitive life stages may have profound effects on development and reproduction for multiple generations. The array of pharmaceuticals in use for both humans and animals will continue to diversify and grow with changing use patterns in human populations and animal production facilities. Rapid developments in the pharmaceutical industry will also continue to quickly add to the vast number of chemicals already entering the environment. Due to the ever-increasing potency and specificity of pharmaceuticals, new substances may be of even greater concern for the environment.

The sources, distribution, fate and exposure in the environment of this wide variety of biologically active substances are not currently well documented in Canada or elsewhere. The ecological and human health consequences of exposure to these substances, their metabolites or products (e.g. anitmicrobial resistance) needs to be determined to allow for scientifically sound risk assessments and the development of appropriate risk management strategies. The regulatory authority for environmental assessment of these substances currently falls under CEPA 1999

This workshop was developed from the recommendation of a recent federal workshop and the recently formed Interdepartmental Work Group on the Environmental Impact of Therapeutic Products in Canada. Health Canada and Environment Canada jointly sponsored this multi-stakeholder scientific workshop, in Niagara-on-the-Lake, Ontario, Feb, 24-27, 2002, to facilitate the discussion of the issue and ensure the widest possible consultation on establishing future research directions and priorities. The main objectives of the workshop were:

- To review the state of knowledge in a Canadian context.
- To identify knowledge gaps for risk assessment, risk management and regulation development.
- To prioritize research needs.
- To identify a collaborative path forward.

The workshop was designed as a combination of formal presentations, breakout groups and round table sessions addressing specific questions, and general plenary discussions. The informal setting was selected to help facilitate open discussion of the widest possible range of knowledge, concerns and ideas. The participants were specifically invited to represent diverse backgrounds and perspectives. International expertise, both scientific and regulatory, was highlighted throughout the workshop

The outcomes of the workshop will form the basis for a scientific review of the issue and enable the identification of major knowledge gaps and research priorities from a Canadian perspective. Moreover, these results will be used to help in the development of a federal agenda to address the issue in Canada and potentially contribute to related international initiatives. The results will also be published in the peer-reviewed literature to maximize the dissemination of the information, conclusions and recommendations to other scientists and the public. These proceedings document the workshop activities, major results, conclusions and recommendations, including prioritization of the major research needs.

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Detailed contact information available in later section.

Workshop Agenda

Co-Chairs: Mark Servos (Environment Canada) and Elizabeth Innes (Health Canada)

Sunday

16:00 Registration
18:00 Dinner
19:30 **Welcome**
19:40 **Introduction** *(Elizabeth Neilsen, Health Canada, and John Carey, Environment Canada)*
20:00 **Plenary Session: International Perspectives**
Pharmaceuticals in the European environment (*Alfredo Alder, EAWAG, Switzerland*)
Monitoring programs in the United States (*Sheridan Haack, US GS*)
A European perspective on pharmaceuticals in the environment
(*José Tarazona, Scientific Committee on Toxicity, Ecotoxicology and the Environment, European Commission, Spain*)
21:30 Reception

Monday

7:00 Breakfast
8:00 **Opening Remarks** (*Mark Servos, Environment Canada and Elizabeth Innes, Health Canada*)
8:30 **Technical Session I: Pharmaceuticals and Personal Care Products in the Environment: Scientific Understanding, Magnitude and Scope**
Session Chair: Jim Maguire, Environment Canada
Exposure in the Canadian environment (*C. Metcalfe, Trent University*)
Exposure from agricultural sources (*E. Topp, Agriculture and Agri-Food Canada*)
Therapeutants in salmonids in mariculture (*Kats Haya, L. Burridge, B. Hargrave, Department of Fisheries and Oceans Canada*)
Potential effects of pharmaceuticals in the environment
(*G. Van Der Kraak, University of Guelph*)
European research on ecotoxicology of human pharmaceuticals.
(*T. Hutchinson, Astra-Zeneca, UK*)
10:00 Charge to the Breakout Groups
10:15 Coffee Break
10:40 Breakout Group Session I
12:00 Lunch
13:00 Breakout Groups Session I (*continued*)
16:00 Breakout Reports/Discussion
Session Chair: Joseph Given, Health Canada
18:00 Dinner
20:00 **Plenary Session: International Perspectives on Assessing the Risk of Therapeutic Products in the Environment**
Session Chair: Joseph Given, Health Canada
Assessing the environment risk of substances under the US Food and Drug Act.

(*Nancy Sager and Charles Eirkson, US Food and Drug Administration*)
Assessing veterinary products in the environment in Europe
(*Alex Tait, Veterinary Medicines Directorate, UK*)
The scientific assessment of pharmaceuticals in the environment in the United States (*Virginia Cunningham, GlaxoSmithKline, USA*)

Tuesday

7:00 Breakfast

8:30 **Technical Session II: Assessing and Managing the Risk of Therapeutic Products in the Environment**
Session Chair: Nigel Skipper, Environment Canada
Assessing the pharmaceuticals in the environment: an example
(*Andreas Hartmann, Novartis, Switzerland*)
The Municipal Effluent Strategy (*Jim Smith, Environment Canada*)
Environmental assessment of products used in animal production (*Jean Szkotnicki, Canadian Animal Health Institute*)
CEPA and the F&DA (*Karen Proud and Neil Tolson, Health Canada*)

10:00 Open Discussion/Charge to the Breakout Groups

10:30 Coffee Break

11:00 Breakout Groups Session II

12:00 Lunch

13:00 Breakout Groups Session II (*continued*)

15:00 Working Coffee

16:00 Breakout Reports and Discussion: Session II
Session Chair: Kim Ostapyk, Health Canada

18:00 Dinner

Wednesday

7:00 Breakfast

8:30 **Session III: Prioritization of Research Needs and Path Forward**
Session Chairs: Mark Servos, Environment Canada and Elizabeth Innes, Health Canada

8:30 The Path Forward *John Arseneau, Environment Canada*

8:45 Presentation of Summarized Research Needs and Discussion

9:00 Prioritization of Research Needs

10:00 Coffee Break

10:30 Developing a Collaborative Path Forward.

12:00 Closing *Kevin Keough, Chief Scientist, Health Canada*

12:00 Lunch

Abstracts

Plenary Session I: International Perspectives

Alfredo C. Alder[1], Christa S. McArdell[1], Eva M. Golet[1], Eva Molnar[2], Norriel S. Nipales[2], and Walter Giger[2]. Pharmaceuticals in the Aquatic Environment a Swiss Perspective.
[1]Swiss Federal Institute for Environmental Science and Technology (EAWAG), [2]Swiss Federal Institute of Technology (ETH), CH-8600 Dübendorf, Switzerland.

In recent years, public and scientific concern about the occurrence of pharmaceuticals in the environment has been continuously increasing. Little is known on the risk of low levels of drugs in the environment because pharmaceuticals are not properly addressed by current environmental risk assessment methodologies. Field studies conducted at scale of operating wastewater treatment plants (WWTPs) and watershed of rivers are needed to validate the predicted environmental concentrations with the actual measured environmental concentrations and to assess the environmental risk that pharmaceuticals could possibly pose toward aquatic organisms and water quality. Therefore, to allow a process-oriented interpretation of the fate and behavior of pharmaceuticals in the aquatic environment, mass flows in WWTPs and in surface waters as well as regional studies are performed. Although today's chemical analytical methods allow us to predict the environmental fate and behavior of micropollutants, they give us an insufficient basis to evaluate the effects on organisms and ecosystems. Therefore, new concepts are needed that combine chemical analytical methods and biological endpoints.

Antibiotics are applied in human medicine and for veterinary purposes with different exposure routes for entering the aquatic environment, i.e., through municipal wastewaters and soil run-off. Our studies emphasize human-use antibiotics belonging to the fluoroquinolone, macrolide, and sulfonamide groups. The two most abundant human-use fluoroquinolone antibacterials (FQs), ciprofloxacin and norfloxacin, occurred in primary and tertiary wastewater effluents at concentrations between 250 and 570 ng/L and from 40 to 120 ng/L, respectively. Elimination rates varied between 75 and 85%. On-going work in our laboratory indicates a substantial sorption of FQs to sewage sludge. The fate of FQs was also investigated in watershed of the Glatt River. In the Glatt River up to 18 ng/L of each FQ were determined. FQs in the dissolved fraction were reduced downstream the Glatt River with 15-20 h residence time to a significant extend (66% for ciprofloxacin and 48% for norfloxacin). Thus, subsequent to wastewater treatment, the fate in rivers creates an additional barrier lowering the residual levels of FQs in the aquatic environment. In addition, selected macrolides were measured in WWTPs outflows. Clarithromycin, erythromycin-H_2O, the main metabolite of erythromycin, and roxithromycin, were found in concentrations of up to 330, 200 and 35 ng/L, respectively. Sulfamethoxazole, which is the main human-use sulfonamide, was found in relatively high concentrations of up to 470 ng/L. In order to evaluated whether the environmental concentrations contribute to the maintenance and spread of antibiotic resistance a project on the occurrence of antibiotics and antibiotic resistance was initiated within the frame of a Swiss National Research Program (www.snf.ch/NFP/NFP49/Home_d.html).

In the European project POSEIDON (www.eu-poseidon.com) the focus is on the assessment and evaluation of technologies for the improved elimination of pharmaceuticals and personal care products (PPCPs) in wastewater treatment and drinking water plants. The effect of partial separation of PPCPs from the wastewater stream due to source control by urine separation is been investigated in the EAWAG Project NOVAQUATIS (www.novaquatis.eawag.ch).

Sheridan Kidd Haack. Monitoring Programs in the United States. USGS, Lansing, Michigan, USA.

Little is known about the extent of environmental occurrence, transport, and ultimate fate of many synthetic organic chemicals after their intended use, particularly hormonally active chemicals, personal care products, and pharmaceuticals that are designed to stimulate a physiological response in humans, plants, and animals. One reason for this general lack of data is that, until recently, there have been few analytical methods capable of detecting these compounds at low concentrations which might be expected in the environment. To provide the first nationwide reconnaissance of the occurrence of pharmaceuticals, hormones, and other organic wastewater contaminants (OWCs) in water resources of the United States, the U.S. Geological Survey used five newly-developed analytical methods to measure concentrations of 95 OWCs in water samples from a network of 139 streams across 30 states during 1999 and 2000. The selection of sampling sites was biased toward streams susceptible to contamination (i.e. downstream of intense urbanization and livestock production). This presentation summarizes the results of this study.

Jose V. Tarazona. Environmental Risk Assessment of Human and Veterinary Pharmaceuticals in Europe. A Scientific Perspective. Second Vice-president of the Scientific Committee on Toxicology, Ecotoxicology and the Environment, DGSANCO, EU Commission, Brussels. Director, Department of the Environment. Spanish National Institute of Agricultural and Food Research and Technology, Madrid, Spain.

This presentation focuses on the current status of the Environmental Risk Assessment of human and veterinary pharmaceuticals in the European Union, the discussions on this issue, and the results of some on-going research and regulatory activities. Accordingly, it is structured in three different parts.

First, the current regulatory status and its technical development as guidance documents (CVMP, 1997; CPMP, 2001) are presented. Environmental Risk Assessments are regulated for new veterinary medicines since 1998. The responsible agency, EMEA, is currently developing a guidance document for human medicines, which up to now are not regulated regarding environmental risks. The conceptual models, analysis plans and decision triggers of EMEA proposals are presented and discussed in comparisons to the European risk assessment for industrial chemicals and pesticides.

Second, a scientific evaluation of the EMEA documents is presented. This evaluation summarises the outcome of three main sources:

- The opinion of the Scientific Committee on Toxicology, Ecotoxicology and the Environment (CSTEE, 2001) on the EMEA draft document on ERA of human pharmaceuticals, adopted in June 2001;
- The CSTEE opinion on effect and risk assessment for terrestrial ecosystems, adopted in November 2000; and
- The on-going discussions under the Working Group on Environmental Risk Assessment associated to the Task Force for Harmonisation of the Risk Assessment Procedures created by the Scientific Steering Committee.

The CSTEE confirmed the need for an environmental risk assessment of human pharmaceuticals. Although the available information is scarce, data suggest that certain pharmaceuticals appear in the environment at higher concentrations than those expected to be safe. The CSTEE was also

critical with the current proposal, which include an initial step based exclusively on exposure assessments. The CSTEE argued that a risk can only be characterised by comparing exposure and effects, therefore, the decision of low risk on the bases of fixed exposure triggers without information on the toxicity of the chemical cannot be scientifically supported. In addition, the selected triggers are not protective enough even for the pharmaceuticals for which ecotoxicity data are available. The need for harmonisation among the different risk assessment protocols was also suggested. This task is currently under discussion by an ad-hoc Task Force. In the draft document, different levels of harmonisation for environmental risk assessment are proposed. Several aspects focus on the application of the scientific basis of ERA and will require further research. These aspects include the selection of the margins of safety, use of probabilistic approaches, interpretation of higher tier studies, etc. The difficulties are particularly important for terrestrial ecosystems, which are a key element in the case of veterinary medicines. The CSTEE suggested an integrated approach for assessing terrestrial ecosystems, which can be applied to pharmaceuticals. The harmonisation of procedures and terminology has less scientific relevance, but it is critical for guarantee transparency and proper risk communication. In the EU system, this aspect is particularly problematic in the case of pharmaceuticals, where different terms are used in the risk characterisation for expressing the same concept.

Finally, some practicalities and suggestions for the future, emerging from both the implementation of the CSTEE opinions (Tarazona and Vega, 2001; Tarazona et al., 2002) and the results of a specific EU research project, ERAVMIS: Environmental Risk Assessment of Veterinary Medicines in Sludge, are presented. This include new conceptual models for assessing the risk of veterinary and human pharmaceuticals on terrestrial ecosystems, as well as the development of new assessment tools, such as the MultiSpecies Soil Systems (MS·3) which offer the possibility of a more realistic assessment, under controlled laboratory conditions, than the standardised test.

Acknowledgements

This paper has not been discussed at the CSTEE/SSC-Task Force for Harmonisation, and therefore, presents exclusively the author's views. However, the contributions of the CSTEE/SSC-Task Force for Harmonisation members have been indispensable for producing this opinion, and therefore the author acknowledge the contribution of all members, and particularly the chairs and members of the working groups responsible for getting the information and producing the first drafts. Some results have been obtained in relation to the EU Project ERAVMIS, EVK1-1999-00034P funded by the 5th Research Framework Programme.

References

CPMP (2001) Discussion Paper on Environmental Risk Assessment of Non-genetically modified Organism (Non-GMO) Containing Medicinal Products for Human Use. CPMP/SWP/4447/00 draft corr. London 25 January 2001.

CSTEE (2001) Opinion on Draft CPMP Discussion Paper on Environmental Risk Assessment of Medicinal Products for Human Use [Non-genetically modified Organism (Non-GMO) Containing]. Brussels, 12 June 2001.

CVMP (1997) Note for Guidance: Environmental Risk Assessment for Veterinary Medicinal Products other than GMO-Containing and Immunological Products. EMEA/CVMP/055/96-FINAL. London, 14-16 January 1997.

Tarazona JV, Hund K, Jager, T., S-Salonen M., Soares AMVM, Skaare JU, and Vigui M. (2002) Standardizing chemical risk assessment, at last. Nature, 415, 14.

Tarazona JV, Vega MM (2001) Hazard and risk assessment of chemicals for terrestrial ecosystems. Toxicology (in press).

Technical Session I: Pharmaceutical and Personal Care Products in the Environment: Scientific Understanding, Magnitude and Scope

Metcalfe, C.[1], B. Koenig[1] and X-S. Miao[1], T. Ternes[2] and J. Struger[3]. Prescription and Non-Prescription Drugs in the Canadian Aquatic Environment. [1] Water Quality Centre, Trent University, Peterborough, Ontario, [2] ESWE Institute, Wiesbaden, Germany
[3] Environment Canada, Ontario Region, Burlington, Ontario.

In Europe, a variety of prescription and non-prescription drugs have been identified in the effluents of sewage treatment plants (STPs) and in rivers and streams near discharges from STPs. Chronic exposure of aquatic organisms to drugs in surface waters could induce biological effects that may alter their physiology, behaviour or reproductive capacity. The primary objective of this project was to evaluate the occurrence and concentrations of prescription and non-prescription drugs in the Canadian aquatic environment, including the effluents from domestic sewage treatment plants (STPs) and surface waters near STP discharges. In a survey of the effluents from STPs in 14 Canadian cities, analgesic/anti-inflammatory drugs such as Ibuprofen and Naproxen, as well as the metabolite of acetylsalicyclic acid, salicylic acid, were often detected in the final effluents at µg/L concentrations. The lipid-regulating drugs, Bezafibrate and Gemfibrozil were detected in some samples of influent and effluent samples at concentrations as high as 2.1 µg/L. Comparisons between concentrations of drugs in influent and final effluent samples are consistent with efficient removal of most drugs during sewage treatment, but some drugs, such as Carbamazepine may be relatively resistant to degradation. Samples of surface water were collected in the summer and fall of 2000 at sites in Lake Ontario and Lake Erie, the Niagara River, in Hamilton Harbour and in the Detroit River near the STPs of the city of Windsor, ON. At sites near the Little River STP in the City of Windsor, concentrations of acidic drugs and carbamazepine were relatively constant at 6 sites located at 100 m intervals downstream of the STP. Since the effluent from this STP contributes approximately 50% to the total flow of Little River, high concentrations of drugs in these surface waters were expected. In contrast, in samples of surface water collected downstream of the West Windsor STP, which discharges directly into the Detroit River, concentrations of most drugs declined to concentrations near or below detection limits within 500 meters of the STP discharge. At sites in the Niagara River, Lake Ontario and Lake Erie, concentrations of drugs were generally below detection limits. These preliminary data indicate that concentrations of drugs are high at sites close to the point of discharge from STPs.

Ed Topp. Pharmaceuticals and Personal Care Products: Exposure from Agricultural Sources. Agriculture and Agri-Food Canada, Southern Crop Protection and Food Research Centre, London, Ontario.

This presentation will give an overview of pharmaceuticals of agricultural origin, pathways to the environment, potential consequences, and opportunities for managing risk. Two classes of chemicals that are used in agriculture and that are of potential environmental concern are antibiotics and hormonal growth-promoting agents. Intensive livestock and poultry operations can use substantial amounts of antibiotics therapeutically, prophylactically, or as growth promoting agents. Various types and amounts of antibacterial and antiparasitic drugs are typically employed in different farming systems. The persistence of these chemicals in the gut, during manure storage, and following application to land is extremely variable, and in some

cases poorly characterized. Increased antibiotic resistance in environmental bacteria exposed to agricultural effluents could represent a new reservoir of antibiotic resistance, ultimately of concern for some human therapeutic agents. Antibiotic-resistant environmental bacteria could be enriched by exposure to excreted antibiotic residues, or by the acquisition of mobile antibiotic-resistance determinants carried by excreted gut bacteria. Excreted estrogenic hormones have very low persistence in agricultural soils. It is highly likely that the greatest risk of contamination of surface and groundwater with these agents comes from overland and preferential flow. Opportunities for minimizing environmental exposure to these chemicals could include a reduction in their use, employing waste storage and treatment practices that destroy them, and using manure application methods that minimize preferential and overland flow.

K. Haya[1], L. E. Burridge[1], B. Hargrave[1], S. Waddy[1] and S. Armstrong[2]. Therapeutants Used in the Salmon Aquaculture Industry. [1]Science Branch, Maritimes Region, Fisheries and Oceans, St Andrews, Nova Scotia, [2]Department of Biology, Dahlhousie University, Halifax, Nova Scotia.

Salmon aquaculture is an important renewable resource industry in both the Pacific and Atlantic coast of Canada. In New Brunswick the industry has developed rapidly from a few farms in 1982 to 87 Canadian and 33 American salmon aquaculture sites in 2000 concentrated in relatively small area of Southwestern Bay of Fundy. Production of cultured Atlantic salmon reached 25,000 tonnes ($190M) in New Brunswick in 2000. In British Columbia the industry developed from ten operating farms in 1984 to a peak of 135 farms in 1998 and the production has increased from roughly 100 tonnes in 1980 to 42,300 tonnes in 1998. By 1998 farmed salmon exceeded the wild salmon harvest in both quantity and value. British Columbia is now the fourth largest producer of farmed salmon in the world after Norway, Chile and the United Kingdom.

The salmon aquaculture industry is a major anthropogenic source of waste in southwestern Bay of Fundy. The wastes may be classified as organic or chemical. Organic wastes result from excess feed and faeces that may accumulate in the sediment and lead to eutrophication in the water column and anaerobic conditions in the sediment. Poor water quality and crowded conditions induce stress in caged fish and contribute to impaired growth and predispose them to disease. This, in turn, necessitates increased use of chemical therapeutants. For example, this area recently experienced sea lice infestations and infectious salmon anemia, a viral infection. Pesticides are being used to combat sea lice infestations and disinfectants help to prevent the spread of the virus.

Some of the pesticides that are used for the treatment of sea lice infestation of caged salmon are in-feed additives and are regulated by the Veterinary Drugs Directorate of Health Canada. For example, ivermectin and emamectin benzoate are currently in use in New Brunswick. In laboratory studies these therapeutants have be found lethal to crustaceans but their impact on wild populations living near salmon aquaculture sites require further research.

A number of antimicrobials are approved for use in salmon aquaculture. In New Brunswick in-feed preparation of oxytetracycline is the antimicrobial of choice. It is used generally to treat non-specific sores on caged salmon. Concerns regarding the use of antimicrobials in aquaculture include, presistance, residue and effects on wild indigenous species living near the salmon cages, development of resistance and the promotion of antibiotic resistant strains of microorganisms. Resistance to oxytetracycline was found in aerobic bacteria cultured from surface sediments

collected at, and near, but not distant from salmon aquaculture farm sites in the Western Isles Region of the Bay of Fundy.

Glen Van Der Kraak and Andrea Lister. Environmental Pharmaceuticals and their Potential to Elicit Physiological Changes in Non-Target Aquatic Species. Department of Zoology, University of Guelph, Guelph, Ontario

The recent detection of pharmaceutical compounds in Canadian surface waters has led to speculations regarding their potential to affect aspects of development, growth, and reproduction of non-target aquatic species. This concern is justified given that evidence has accumulated over the past decade demonstrating effects of low concentrations of hormonally-active drugs (e.g., ethynylestradiol) on the reproductive endocrine systems of fish. Assessments of the physiological impacts of drugs on non-target species of wildlife may encounter challenges beyond those associated with priority chemicals (e.g., pesticides, metals) because human and veterinary pharmaceuticals have been formulated specifically to interact with biological receptors or signal transduction pathways that are critical to physiological processes. In addition, the high biological activity of drugs at low doses coupled with the possibility that exposures may be continuous adds to the concern that pharmaceuticals may affect the overall fitness and survival of aquatic species. The broad suite of chemical classes detected in the environment introduces an interesting challenge to scientists in this emerging field of study- numerous physiological endpoints will have to be examined that span different biological systems (e.g., neuroendocrine, reproductive, immune) in order to obtain a holistic view of whether or not drug-induced physiological changes impact the overall fitness of environmentally-exposed species.

Current knowledge of some of the biochemical mechanisms involved in pharmaceutical actions can be used to direct the initial research efforts in order to examine physiological responses that are important in developmental and reproductive processes. For example, there is evidence that pharmaceuticals (e.g., hormone agonists and antagonists) that interact with various aspects of endocrine physiology may be of concern. There is limited evidence suggesting that hypolipidemic drugs (e.g., clofibric acid) that alter cholesterol levels and nonsteroidal anti-inflammatory drugs (e.g., indomethacin) that inhibit prostaglandin synthesis may exert effects on reproductive endocrine processes. Likewise, developmental processes may be affected by compounds that interact with retinoic acid receptors or alter vitamin A status. The risks posed to wildlife by anti-neoplastic drugs (e.g., chemotherapy agents) and their potential to cause subtle and cumulative genetic changes, or drugs that alter neurobehaviour (e.g., antidepressants like the selective serotonin reuptake inhibitors) have not yet been explored. Although there are physiological endpoints that can be used to detect the potential effects of selected drugs, there is a large number of compounds that exert their activities through mechanisms for which we do not have appropriate endpoints developed in wildlife species.

Plenary Session II: International Perspectives on Assessing the Risk of Therapeutic Products in the Environment

Nancy Sager[1] and Charles Eirkson[2]. Assessing the Environment Risk of Substances Under the US Food and Drug Act. [1]Office of Pharmaceutical Science, Center for Drug Evaluation and Research (CDER), US Food and Drug Administration, [2]Center for Veterinary Medicine (CVM), US Food and Drug Administration, Rockville, MD.

The National Environmental Policy Act of 1969 (NEPA) requires all Federal agencies in the United States to assess the environmental impacts of their actions. The Center for Drug Evaluation and Research (CDER) and Center for Veterinary Medicine (CVM) are required under NEPA to consider the environmental impacts of approving drug applications as part of their regulatory process. FDA's regulations at 21 CFR part 25 specify that environmental assessments (EAs) must be submitted as part of certain new, abbreviated, and investigational drug applications unless the application qualifies for categorical exclusion. FDA has over ten years experience in performing environmental assessment reviews.

Alex Tait. Environmental Risk Assessment of Veterinary Medicines in the EU. Veterinary Medicines Directorate, Alderstone, Surry, United Kingdom.

In the European Union (EU) the legislation covering the authorisation of veterinary medicinal products (VMPs) is set out in Directive 2001/82/EC. This legislation is implemented at EU level by the Committee for Veterinary Medicinal Products (CVMP). The legislation states that all VMPs require a Marketing Authorisation (MA) before they can be placed on the market and they must satisfy the criteria of quality, safety and efficacy to be granted a MA. The requirement for assessment of environmental safety was introduced into the legislation by Directive 92/18/EC which amended the original Directive in 1993. Since that time data on ecotoxicity have been required as part of the safety submission for a MA.

The Directive states that the environmental assessment should be carried out in two phases. In the first phase the extent of environmental exposure is estimated while in the second phase the fate and effects of the active residue (parent and/or metabolites) are assessed. The basic framework provided by the Directive has been elaborated by guidelines published by the CVMP. These guidelines provide guidance to both applicants and to the regulators on exactly how the assessment of environmental safety should be carried out. The CVMP guidelines were introduced in 1997 and mirror the Directive in that the assessment procedure is carried out in two phases. Recently the original Phase I guidelines were replaced by a new Phase I guidance developed under the VICH procedure. Both the Phase I and Phase II guidelines use a decision tree approach. In Phase II the assessment is carried out using a tiered approach. The assessment will only proceed to Tier B if some risk remains after the assessment at Tier A.

A Phase I assessment of environmental safety has to be carried out for all products. The intention of the Phase I assessment is to remove from the requirement of more detailed assessment those VMPs whose use does not result in extensive exposure of the environment. No specific environmental data are required to complete the Phase I assessment. The Phase I guidance provides a set of criteria and triggers, based on a decision tree, which are used to decide if exposure of the environment is extensive or not. Exposure of the environment is not considered to be extensive for dog and cat products, for products used in a small numbers of animals and for products where the predicted environmental concentration (PEC) of total residue in soil is <100 µg/kg. Models are available for calculation of the PEC which give some consistency to the calculations. Two categories of product move straight from Phase I into Phase II without any assessment. These are products used as ecto- or endo-parasiticides on animals at pasture and fish medicines which are added directly to the environment.

For products which enter Phase II the assessment is carried out in a stepwise fashion and the basic data required are similar to those needed for the assessment of other chemicals and pesticides. However, the major difference between environmental assessment of VMPs compared with either pesticides or other chemicals is the fact that VMPs, in most cases, enter the environment in excreta of the treated animal. Exceptions are products used as ecto-parasiticides

which are applied topically and fish medicines which are administered in feed or added to water. Depending on the extent of metabolism of the drug by the target animal the residue may consist entirely of parent compound or may consist mostly of a major metabolite with little parent present. The Phase II investigation should concentrate on the major residue which enters the environment although in practice this is not always possible.

In Phase II, Tier A, for products used in farm animals, data on the fate and effects of the residue in soil are obtained in laboratory studies carried out to appropriate guidelines such as Organization for Economic Co-operation and Development (OECD). Data on degradation of the residue in soil and its adsorption/desorption properties will identify the environmental compartments at risk and will provide information on persistence of residue. Using these data together with information on how the product is used enables the estimation of exposure of different environmental compartments by calculation of a PEC value. Effects data produced in the laboratory are compared with the PEC for soil and further assessment is only required if the PEC:effects ratio exceeds a trigger value. For the aquatic environment the effects data from the most sensitive species amended by an assessment factor is used to determine a predicted no effect concentration (PNEC). This PNEC is compared to the PEC and additional information is only required if the PEC:PNEC exceeds 1. If the Tier A assessment indicates that some risk remains then the assessment moves to Tier B where more data specific to areas of concern are produced. In Tier B the additional data are used to further characterise the risks to the environment. Tier B studies tend to focus on specific concerns remaining about the environmental risk such as the effects of persistent residue on soil organisms, field effects on dung fauna, studies on terrestrial vertebrates and studies on aquatic and sediment organisms. Examples of the assessment procedure for intensively farmed animals and those kept at pasture will be given in the presentation.

The assessment of fish medicines begins in Phase II as the VMP is added directly into the environment. As for terrestrial animals the process is carried out in stages and is based on a decision tree. In the first stage some basic physico-chemical studies and effects studies on aquatic organisms are carried out. The results are compared to trigger values and if the triggers are exceeded further studies are required. In the second stage the fate of the VMP in the water is examined, its adsorption to sediment and degradation in water. In addition the potential for bioaccumulation is investigated. After generation of these data the environmental risk is assessed. This process relies more on scientific judgement than on the use of trigger values. If the risk is considered to be anything other than low then further studies are requested. These studies could include fate in sediment, dispersion, microcosm or mesocosm studies and field studies. In the final analysis the risk assessment is made using scientific expertise. An example of the assessment procedure for a fish medicine in feed will be discussed in the presentation.

In the future the production and implementation of the VICH Phase II guidelines is a key aim of the regulators and industry in the area of environmental assessment. In the EU there is a proposal for the production of a 'technical handbook' for use by EU experts when assessing environmental safety. Such a document is considered important to ensure consistency among the experts in each EU country. In terms of research into aspects of environmental assessment this is not an area where regulatory agencies frequently venture. However, there are some research projects either beginning or already underway which should be mentioned. These are the development of computer simulations for movement of residue to groundwater and surface water, the development of testing methods for effects on dung fauna and the monitoring of fish medicines in the environment after authorisation of VMPs. The latest developments in these projects will be given in the presentation.

Virginia L. Cunningham. The Scientific Assessment of Pharmaceuticals in the Environment in the United States. Environmental Product Stewardship, GlaxoSmithKline, King of Prussia, PA, USA.

Generating environmentally relevant physical, biological and ecotoxicological data for human pharmaceutical compounds, and assessing these data from a risk mitigation and management perspective, is carried out in increasing detail during the drug development process. A key to the success of this approach is an understanding of which parameters are most useful for the various assessments that are conducted. For example, there are generally different data needs to assess potential impacts from the introduction of active pharmaceutical ingredients into the environment through manufacture of clinical and commercial products, as compared the impacts from patient use and excretion into wastewater treatment plants, and then into the environment. Impacts from the direct introduction into the environment from accidental releases, or in areas without sanitary treatment may also require special data. Careful consideration of the data required to make assessments throughout the life cycle of the drug facilitates efficient, cost effective generation and use of the data. It also enables the assessment methodologies to be tailored to the release scenarios likely to be encountered when the new drug product is manufactured and marketed.

Pharmaceutical compounds often pose technical challenges from an environmental risk assessment perspective. In general, they tend to be large, multi-functional, ionizable, or at the very least, highly polar chemicals. As a result of these characteristics, many models historically used to estimate environmental properties or partitioning behavior are not well suited for use with pharmaceutical compounds, and care must used in evaluating data generated by them. This presentation will review the key data required to assess environmental risk of human pharmaceutical compounds and selected emerging fate modeling techniques. These models are beginning to facilitate early guidance on testing strategies and provide better predictions for potential environmental concentrations. These predicted concentrations, when used with estimates of no-effects levels for human health and the environment allow credible early assessment of potential environmental impacts.

Technical Session II: Assessing and Managing the Risk of Therapeutic Products in the Environment

Andreas Hartmann, Ya-Juin Chou, Zdenek Assessing Pharmaceuticals in the Environment: An Example for the EU. Novartis Pharma Product Safety Branch, Basel, Switzerland.

Western Europe accounts for about 25% of the global pharmaceutical market (North America 50%). Between 1994 and 2000, about 40 new chemical entities have been introduced to the global market each year. Environmental issues were only recently regarded a potential problem. The competent Regulatory Agency in the EU is EMEA (European Agency for the Evaluation of Medicinal Products). In the years 1994/1995, several EU working groups discussed various test proposals, with the first idea of basing drug ERAs on the existing guidelines for industrial chemicals. The currently proposed used guideline is the "Draft EMEA/CPMP discussion paper on Environmental Risk Assessment of Medicinal Products for Human Use" (January 2001).

As a case study for human drugs, an ERA of the antiepileptic Carbamazepine (CBZ, Tegretol®) is presented, according to the actually proposed ERA guideline. Since the patent expiry of

Tegretol®, generic products are increasingly present on the carbamazepine market. However, the available monitoring data allow a realistic assessment of the environmental exposure.
Human metabolism: CBZ is excreted to 1 % unchanged, to 2 % as the active metabolite and to 30 % as inactive metabolites and glucuronides. As a worst case, 33% of an applied dose may therefore be regarded as pharmacologically active when reaching the aquatic environment through an STP. Exposure situation: Typically measured environmental concentrations (MEC's) of CBZ in the EU are 2.1 µg/L in treated wastewater effluents* and 0.5 µg/L in surface waters **. CBZ was not detectable in drinking waters (<10 ng /L ***). These data are in good agreement with exposure predictions based on production figures. Since the vapour pressure of CBZ is very low (<10E-7 hPa) and sorption to sludge is not expected to occurr to a significant extent (Kow = 1.76, 7 % removal in STP (Ternes 1998), the aquatic compartment can be regarded as the most relevant for the ecological assessment of CBZ. Degradation: CBZ does not show significant degradation in the 28d-OECD 301E ready biodegradability assay and has been shown to be scarcely eliminated in German sewage treatment plants (7% , Ternes 1998). Photolysis has recently been shown to occur under environmental conditions***.

Ecotoxicology: CBZ has a 96h-LC50 of 43mg/l towards zebra fish (brachydanio rerio), a 24h-EC50 of 92 mg/L towards Daphnia magna and a 3h-EC50 of >320mg/l in the sludge respiration inhibition assay (OECD 209). Furthermore, the acute and chronic toxicity of CBZ towards algae has recently been assessed in a non-standard assay****. An acute 96h-NOEC of 20 mg/L and a chronic NOEC of 19 mg/L (highest tested concentration) was found. Together with the missing evidence for bioaccumulation of CBZ in the algae, these data suggest only negligible effects of CBZ towards algae under chronic environmental exposure conditions.

Applying an uncertainty assessment factor of 1000 to the lowest available acute effect concentration (43 mg/L in fish), as suggested by the guideline, yields a predicted no effect concentration (PNEC) of 43 µg/L. The resulting risk ratio based on the measured exposure data for surface waters (0.5 µg/L) results in a MEC/PNEC of 0.01. According to the guideline, no further assessment is therefore necessary, since the trigger limit of 1 is not reached.

To take this a step further, environmental concentrations are compared with human plasma concentrations under the recommended daily dose (RDD). Plasma concentrations are between 4-12 µg/ml (PDR, Swiss drug compendium). If plasma levels in environmental species are assumed to reach the MEC, the minimal pharmacological safety factor for target effects under chronic exposure to surface water is between 8-24'000. The same safety range applies if epidemiological data are taken into account, the lead effect being human teratogenicity at clinincal doses (CBZ is e.g. five times safer than valproate). There is no conclusive evidence for carcinogenic effects, and bacterial and mammalian mutagenicity studies produced negative results. Overall, this extended assessment corroborates the finding that CBZ is not of immediate concern for the aquatic environment.
* median (n=30), Ternes 1998, **mean 90th percentile (n=222) from Sacher et al. 1998, Ternes 1998, ***Mons et al (2000), ****Andreozzi et al., Water Res, in press.

Jim Smith. Environment Canada's Municipal Wastewater Effluent Strategy 2002.
Environmental Protection Branch, Ontario Region, Environment Canada, Toronto, Ontario

The presentation summarizes recent information which has led to an increased priority for the control and prevention of municipal wastewater effluent discharges to the environment. Environment Canada's 4-Part Strategy is outlined for this sector, as well as a variety of tools

and instruments available to the federal government to meet its regulatory obligations, plus some of the challenges in addressing the complex issue of wastewater management in Canada.

Jean Szkotnicki. Environmental Assessment of Pharmaceuticals Used in Animal Production. Canadian Animal Health Institute, Guelph, Ontario.

The Canadian Animal Health Institute (CAHI) is the trade association representing the manufacturers and distributors of animal medications in Canada. Since mid September 2001 animal pharmaceuticals must under go an environmental assessment. The animal health industry wants to provide input to Health Canada in developing regulations that address environmental safety while being manageable for industry. Critical to industry is that the regulations be predictable, have defined endpoints, be cost effective and are equivalent to other jurisdictions, particularly the U.S., our largest trading partner relative to foods of animal origin.

Export markets are important to many food animal sectors. It is therefore important that our food animal producers and veterinarians have access to the same management tools as that of competing nations. The VICH process provides a logical process for Canada to pursue its EA work. The VICH ecotoxicology working group has signed-off on a Phase I guideline which addresses categorical exclusion parameters or an EA that addresses only environmental exposures. Phase II guidelines, which will have greater data requirements, are now under discussion. Industry believes the Phase II guidelines require defined endpoints. It is important that Canada be a part of this overall process; we cannot afford to reinvent the wheel. Further, Health Canada must not develop EA regulation in isolation of addressing issues of unlicensed drug use in Canada. Canada cannot be seen to support two sets of rules – one for licensed pharmaceuticals and another for unlicensed.

In closing, the animal health industry is not adverse to doing EA's if they are justified and if the product is able to support the research and development investment needed to do the work.

Karen Proud[1] and Neil Tolson[2]. CEPA and the F&DA. [1]Health Products & Food Branch, Health Canada, [2]Environmental Assessment Unit, Healthy Environments and Consumer Safety, Health Canada, Ottawa, Ontario.

Health Canada is undertaking the development of new environmental assessment regulations for substances in products regulated under the Food and Drugs Act (F&DA), as part of its mandate to improve and protect the health and safety of Canadians and its shared federal responsibility for the protection of the environment. The responsibility for coordinating this effort lies within the Office of Regulatory and International Affairs, in the Health Products and Food Branch of Health Canada.

An Environmental Assessment Unit (EAU) has been established in the Healthy Environments and Consumer Safety Branch of Health Canada and is currently conducting environmental assessments under the Canadian Environmental Protection Act (CEPA) and New Substances Notification Regulations (NSNR). The EAU consists of biologists and chemists with a wide range of backgrounds and experience. The EAU evaluates data to determine the impact of the release into the environment of substances new to Canada that are regulated under the F&DA, e.g., pharmaceuticals and veterinary drugs. Major activities include the refinement of assessment

tools, conducting assessments of notification under the NSNR under CEPA and the development of new regulations that are appropriate for F&DA

Breakout Sessions

The participants from different sectors and disciplines were broken into small groups to facilitate discussion of specific issues and questions. The following questions were presented to the groups to guide their discussion. Each group was assigned a chair to facilitate the discussion and a reporter to record the major conclusions and recommendations. The conclusions of each breakout session were presented in a general plenary session. The presentations, discussion and breakout reports were synthesized for each of the questions and general conclusion highlighted. Each group was asked to examine the questions from a slightly different perspective:

Group 1	Human exposure and effects.
Group 2	Environmental impacts.
Group 3	Wastewater management.
Group 4	Agricultural environments and runoff.
Group 5	Environmental exposure and methods.

Questions for Breakout Session I: Pharmaceuticals and Personal Care Products in the Environment: Scientific Understanding, Magnitude and Scope

- Is this issue a concern for Canadian ecosystems or human health? Can you rank the level of concern relative to other environmental issues? *All Groups*
- Are analytical methods adequate to determine exposure to the environment or humans? Are standardized methods required or desirable? *G1,5*
- Is there significant exposure in the environment? What are the major sources/loadings? Can you rank the importance of each source? *All Groups*
- What are the major pathways of environmental exposure to ecosystems or humans? *G2,4,5*
- Which substances currently represent the highest potential for exposure or effects? *All Groups*
- Which substances or groups have the potential to cause harm? *All Groups*
- Which substances or groups require the most attention? Why? *All Groups*
- What environments, populations (ecosystems/humans) are most exposed? Which are most at risk? *G2,3,4*
- Are there ecosystems or populations that are particularly sensitive or at risk because of their unique characteristics (e.g. early life stages, children, aged, sick, etc.)? Why? *G1,2,3*
- What types of effects are predicted? *G1,2*
- What are the approaches or tests most appropriate for screening or assessing the potential effects? *G1,2,5*
- What are the major research needs? Can you prioritize them in the order to which attention should be given? *All Groups*

Questions for Breakout Session II: Assessing and Managing the Risk of Pharmaceuticals and Person Care Products in the Environment.

Assessing the Risk

- Are there activities internationally that will influence Canadians (OECD, US, EU, harmonization, etc)? List them. *G1,2*
- Is there adequate knowledge and data on exposure (*G 1,2,5*) and effects (*G 3,4*) to make scientifically sound risk assessments and scientifically defensible regulations in Canada?
    - What knowledge/data are needed?
    - Are the current methods/endpoints adequate? Why?
    - Are new methods/approaches and endpoints required? If so what are they?
    - Are current approaches adequate for new vs. existing substances?
    - In what time frame is it needed.
    - Prioritize the research needs for risk assessment and regulation development.

Managing the Risk

- Are monitoring programs needed? If so what needs to be included? *All Groups*
- Can the effectiveness of current or proposed regulations be assessed or monitored? *G1,2,5*
- How effective are current risk management options: municipal treatment, Best Management Practices for agriculture, drinking water treatment? *G1,3,4*
- Can/should risk management options be developed and what research is needed? *G1,3,4*
- What actions need to be taken in the short term and long term to reduce exposure and potential risks? *G2,4,5*
- Are there opportunities for collaboration among various research groups? *All Groups*
- Prioritize the research needs for risk management. *All Groups*

Summary of Assignment of Participants to Breakout Groups

	Group 1: Human exposure and effects	Group2: Environmental impacts	Group 3: Wastewater management	Group 4: Agricultural environments and runoff	Group 5: Environmental exposure and methods
Rooms	**Loyalist**	**Somerset**	**Balmoral**	**Magnolia**	**Trillium**
Chair 1	**Robert White**	**Glen Van Der Kraak**	**Don Bennie**	**Ed Topp**	**Chris Metcalfe**
Chair 2	**Karen Proud**	**Neil Tolson**	**Phillipa Cureton**	**Nigel Skipper**	**Andy Atkinson**
Recorder	Mary Ellen Starodub	Ève Dussault	Caroline Mimeault	Kim Ostapyk	Andrea Lister
	Nancy Sager	S.K. Ho	Fance Lemieux	Charles Eirkson	Sheridan Haack
	John Blatherwick	Karen Kidd	Tony Ho	Alex Tait	Bill Lee
	Hugh Davis	Jack Bend	Carlos Montreal	Vance Treaudeau	Andrew Beck
	Kyra Patterson	Alan Penn	Peter Seto	Jean Szkotnicki	Sean Backus
	Johnathan Tigner	Nick Fendiger	Albert Van Roodselaar	Colin Rousseux	Andy Atkinson
	José Tarazona	Jim Sherry	Alfredo Alder	John Headley	Allan Godfrey
	Barbara McElgunn	François Gagné	Son Chau	Linda Webster	Norm Neumann
	Georgine Pastershank	Sean Richards	Dave Edge	John Struger	Flora Ratpan
	Tom Edge	Elizabeth Nielsen	Kent Burnison	Mark McMaster	Marvin Faber
	Adel Shalaby	Karl Carter	Tom Moon	Kats Haya	Ruban Gandia
	Leonor Alvarado	Pierre Meurice	Jim Smith	Joseph Robinson	David Blakey
	Joseph Given	Lisa A. Constantine	Michel Beland	Tom Hutchinson	Katharine Leitch
	Adam Socha	Andreas Hartmann		Sandra Schwartz	Virginia Cunningham
	Diane Koniecki	Scott Brown			Jim Maguire

Note that breakout groups were selected to ensure a variety of perspectives and balance. Participants may have moved among groups during the workshop.

Synthesis of Breakout Session Reports

Breakout Session I: Pharmaceuticals and Personal Care Products in the Environment: Scientific Understanding, Magnitude and Scope

The objective of Breakout Session I was for participants to review the level of understanding of the science of exposure and effects of PPCPs in the environment from the perspective assigned to each specific group. The assigned questions were designed to lead the group discussions with the ultimate goal of identifying data gaps and scientific research needs.

General Conclusions

- The issue of PPCPs in the Canadian environment needs to be taken seriously given their widespread use, quantity, wide variety of products released to the environment and the known potential of many drugs to interact with biological systems.
- There is great uncertainty regarding the potential human health and ecological effects of low levels of PPCPs in the environment.
- There is an immediate need for a sophisticated screening strategy to prioritize PPCPs of greatest concern to human health and ecological health on the basis of their physical-chemical properties, environmental fate and bioaccumulation potential, sensitive endpoints of greatest concern, sensitive life stages, populations, and sensitive non-target species and ecosystems.
- There is a need for a National strategy to address the human health and ecological significance of PPCPs in the Canadian environment.
- There is an immediate need for better problem definition in a Canadian context with respect to identification of types and volume use of PPCPs, wastewater treatment and disposal practices, and agricultural practices across Canada to estimate loadings to the environment on a regional basis.
- There is an immediate need for a better understanding of the fate and effects of PPCPs in Canadian wastewater treatment systems, septic systems, drinking water and the receiving environment.
- There is a need to identify sensitive sentinel species for environmental effects monitoring programs and laboratory testing, and to identify sensitive human populations.
- To achieve the above needs, new and improved analytical methods for the determination of exposure and effects of PPCPs at environmentally relevant concentrations and exposure scenarios will be required.

Summary of the Responses to Specific Questions

- **Is this issue a concern for Canadian ecosystems and human health? Can you rank the level of concern relative to other environmental issues?** *All groups addressed this question.*

All groups responded (yes) that PPCPs in the environment are recognized as a concern for the health of Canadians and Canadian ecosystems.

However, it is generally agreed that the available data to characterize exposure and potential health effects is insufficient to definitively comment on the level of concern warranted by PPCPs in the environment or to assign a relative ranking to this issue versus other environmental issues (e.g. global warming and GMOs). The collective descriptor PPCPs encompasses a vast number of active and in-active chemical ingredients, some of which by design target biological functions and receptors (e.g. pharmaceuticals such as, cardiac drugs, antidepressants, natural and synthetic hormones, antibiotics) while others are unintended to interact with biological systems (e.g. personal care products such as, fragrances, stabilizers and emulsifiers). There is general consensus that the issue of PPCPs in the environment needs to be taken seriously given the pervasive nature of these substances, their widespread use, volume quantity and wide range of products continually released to the environment and their potential to interact with biological systems. At the present time risk communication should stress that there MAY be a health risk but that there is no certainty at this time given the current level of understanding of the issue in a Canadian and international context. There is an immediate need to prioritize concerns as they relate to types of PPCPs of greatest concern, sensitive endpoints of greatest concern, characterization of sensitive individuals and life-stages, non-target species, and ecosystems.

- **Are analytical methods adequate to determine exposure to the environment or humans? Are standardized methods required or desirable?** *Groups 1 and 5.*

Human Exposure

Are analytical methods adequate to determine exposure?

It was unanimously agreed that present analytical methods are inadequate to determine PPCPs exposure of humans via drinking water, swimming, and other water reuse practices. Current methods used by regulators to assess potential human health risk through direct exposure to pharmaceuticals and personal care products as it relates to intended use practices are considered adequate to protect human health of the user. However, these methods are not designed to address unintended long-term low level indirect exposure through water reuse practices. Nor do they typically assess long-term low level exposure effects on non-target human populations such as formula fed infants, in-utero fetus, children, the elderly, or immunologically compromised individuals.

Are standardized methods required or desirable?

Standardized methods are both required and desirable to determine levels of human exposure to PPCPs in drinking water, recreational waters and groundwater. Standardized analytical chemistry methods are required that use detection limits that are environmentally and toxicologically relevant to enable risk assessment of PPCPs in the environment. Analytical chemistry methods are needed to detect the parent chemicals, their metabolites of humans and animals, microbial metabolites of activated sludge treatment, and their environmental degradation products. The determination of exposure of Canadians and the environment to PPCPs needs to consider the diversity of municipal STPs across Canada. Since PPCPs in wastewater, surface waters, ground waters and drinking waters occur as complex mixtures there is a need to develop sophisticated screening methods and to modify existing methods to address the unique characteristics of these substances. Through such a screening process classes and types of PPCPs of greatest concern could be prioritized and surrogate chemicals selected as representative chemicals of each group. A strategy to look for effects in the receiving environment developed in concert with traditional analytical chemistry methodologies is proposed as a biological analytical tool. A similar approach is being advocated in the EU. Finally, it was reiterated to caution against the approach of "chasing the last molecule" but to focus on the human health and ecosystem health significance of environmental levels of PPCPs recognizing their uniqueness in comparison to traditional industrial chemicals.

Environment Exposure

Are analytical methods adequate to determine exposure?

No, analytical methods are not adequate for all PPCPs and their metabolites. With respect to the aquatic matrices (water, effluent) there are currently available in the public domain analytical chemistry methods for some PPCPs. There are considerably fewer methods available in the public domain for PPCPs in sludge, sediment and biological tissues.

Are standardized methods required or desirable?

Overall there is an immediate need for the development of analytical methods for PPCPs in all environmentally relevant matrices. This includes a need for analytical methods for the detection of the parent chemical, human and animal metabolites, microbial metabolites of activated sludge, and their environmental degradation products. Some participants are of the opinion that the development of standardized methods will be a long-term process. There is a need to develop a strategy to look for evidence of exposure in the receiving environment as a biological analytical tool; this biological indicators approach is being advocated in the EU. Finally, the primary analytical needs identified by participants of group 5 are:

- Surrogate standards representative of various classes and types of PPCPs.
- Standard reference materials for each class and type of PPCPs.
- QA/QC capability within a designated agency.
- Biological indicators of exposure.

- **Is there significant exposure in the environment? What are the major sources/loadings? Can you rank the importance of each source?** *All groups.*

Significant exposure:
Although PPCPs have been detected in the environment, the toxicological relevance of these findings at the respective concentrations is uncertain, particularly with respect to human health. Some substances have been detected in the environment at concentrations that have been reported to induce biological effects in aquatic toxicity laboratory tests. Further study is warranted.

Major sources/loadings:
Major sources that have been identified include:

- Wastewater effluents of municipal STPs.
- Hospital wastewater effluents.
- Animal production facilities, animal wastes, manure application.
- Aquaculture practices.
- Biosolids disposal management applications (STPs and manures).
- Disposal practices for unused drugs and cosmetics.

Other potential sources that were noted during discussions include:

- Rural septic systems.
- Landfills.
- Universities.
- Military bases .
- Seniors residences.
- Veterinary facilities large and small animal practices.
- Puppy mills (low level antibiotic use).
- Race horse facilities and animal wastes.
- Illicit drug operations, waste disposal and use.

PPCPs cover a wide variety of substances and products. Certain pharmaceuticals may be in greater use than others (e.g. oral contraceptives vs. antineoplastic agents or orphan drugs), as will certain personal care products (e.g. sunscreen products, hand soaps and detergents vs. specialized beauty products) that will determine their relative releases to the Canadian environment. Also, community and regional differences in the volume use related to socio-economics, differences in wastewater treatment technologies, as well as differences in industry and agricultural practices will be reflected in the loadings and type of PPCPs present in the Canadian environment.

It was generally agreed that the data at hand not sufficient to rank known sources relative to each other. Additional information on loading rates, types of PPCPs in terms of their potency, persistence and bioaccumulative potential and measured or expected concentrations is required to do this with any degree of confidence. It is also noted that

new high potency drugs designed to persist in biological systems may be an emerging issue.

4. **What are the major pathways of environmental exposure to ecosystems or to humans?** *Groups 2,4 and 5.*

Discussions of pathways of PPCPs into the environment are focused on waterborne, sludge and soil releases. Major pathways of environmental exposure to ecosystems or humans identified with municipal treatment plants and agricultural practices are:

- Treatment of human sewage and animal wastes in STPs with the subsequent release of wastewater effluents to surface waters; thus resulting in exposure to aquatic ecosystems, and human exposure when surface waters are used as a source of drinking water.
- Application of sludge from municipal treatment plants to agricultural soils, resulting in exposure of terrestrial ecosystems, leaching to groundwater and subsequently to surface waters; thus resulting in potential exposure of aquatic ecosystems, and human exposure when affected groundwater or surface water is used for drinking water.
- Agricultural runoff resulting from low-tech (e.g. pastures) or high-tech (spreaders, compost) manure management; application to soils with movement to nearby surface waters or percolation into groundwater leading to ecosystem and human exposure.

Landfill of unused pharmaceuticals and personal care products and leaching to groundwater may be another pathway. Discussions pointed out that release of PPCPs to the environment through volatilization has not been addressed yet for some products this pathway may be of importance. For example musks are PPCPs that are volatile.

- **Which substances currently represent the highest potential for exposure or effects? Which substances or groups have the potential to cause harm? Which substance or groups require the most attention?** *All groups.*

Basic principles support the rationale that PPCPs, and their metabolites, likely to be of greatest concern are those with:

- a relatively high toxicological potency,
- high bioaccumulative potential,
- high environmental persistence (including potential continuous or repeated exposures),
- and high volume use and release into the environment.

With respect to drugs, those that are high potency, most frequently prescribed or purchased over-the-counter, and are poorly degraded in municipal STPs and septic systems would have the greatest potential for environmental exposure and effects. There is little information on concentrations of personal care products in wastewater effluents and the environment. Information on the potential effects of PPCPs at environmentally relevant concentrations is not well known and more research is needed

Examples of types of PPCPs (for human and veterinary use) that may be of greatest potential concern (not prioritized) include:

- Anti-neoplastic drugs and other high potency specialized drugs.
- Antibiotics and the development of antimicrobial resistance.
- Hormonally active substances (natural and synthetic).
- Antidepressants, neurotransmitters and other psychotherapy drugs.
- Low level mixtures of PPCPs with similar mechanism of toxic action or that induce effects on same target tissue or endpoint.
- Musks and other potentially bioaccumulative substances .
- Analgesics - high volume use.
- Personal care product ingredients – high volume use.
- Cardiac drugs and lipid regulators – high volume use.
- X-ray contrast media – environmental persistence; high volume use.
- Antiparasitics used in agriculture and aquaculture – toxic to non-target invertebrates; high volume use on regional basis.
- Caffeine – high volume use.
- Feed additives – regional high volume use.
- Natural health products – little known about these; popularity and use increasing.
- Antifoulants – regional high volume use.
- Disinfectants, antimicrobials (triclosan) – high volume use.
- Other personal care products.

It was reiterated, throughout the breakout session that the process of identification of PPCPs of greatest concern needs to consider regional information on volume use and release data for PPCPs in addition to their physical-chemical properties governing environmental fate and their relative toxic potency. EU representatives shared their perspective based on experience for the need to develop regional lists of substances that reflect the variance in concentrations of PPCPs in wastewater effluents linked to regional marketing practices. For instance one region may preferentially use certain drugs and personal care products in contrast to another region and this preferential use may be attributed to cultural differences, marketing or economics. EU monitoring studies have captured not only regional differences in PPCPs constituents of wastewater but also variance according to time of day or other periods of time that can be linked to human lifestyle activities and marketing affecting product use.

It is generally agreed that the current level of understanding of the workshop participants was insufficient to target specific substances for immediate attention. In order to do so a more in-depth-review of available information including volume use, physical-chemical properties, environmental fate, structure activity relationships, acute to chronic relationships, effects of long-term low-level exposure in a variety of non-target and target species including humans is required to prioritize substances of concern. Also important to the understanding of the potential health risks of PPCPs in the environment is the identification of PPCPs that have been tested under controlled conditions and found to have no adverse effects at environmentally relevant levels. Finally studies are needed to

describe the dose-response and to elucidate the mechanisms of action for groups of PPCPs.

- **What environments, populations (ecosystems/humans) are most exposed? Which are most at risk?** *Groups 2, 3 and 4.* **Are there ecosystems or populations that are particularly sensitive or at risk because of their unique characteristics (e.g. early life stages, children, aged, sick, etc.)? Why?** *Groups 1, 2 and 3.*

In addressing these questions emphasis is given to the identification of environments and populations that would be expected to receive the greatest exposure on the basis of current understanding of environmental exposure pathways. In terms of identifying those at greatest risk information to characterize the exposure and hazard is needed. Although there is limited information on the hazard of PPCPs, the identification of environments and populations potentially at greatest risk can be surmised from knowledge of the relative sensitivities of life-stages and sensitive populations, information on the intended use of the product and route of entry into the environment. For example, aquatic invertebrates would likely be sensitive to anti-parasitic agents applied in the aquatic environment or released in wastewater effluents; microorganisms would likely be sensitive to antimicrobial agents; developing fetus would likely be sensitive to neuroendocrine disruptors and early life stages may be sensitive to growth modifiers.

In this manner the following environments and populations (ecosystems/humans) are identified as potentially of greatest concern with respect to environmental impacts related to municipal wastewater treatment and agricultural practices.

Ecosystems

- Terrestrial ecosystems: soil fauna including microorgansms; soil fertility; development of antimicrobial resistance; food chain effects - consumers of soil fauna; crops/plants.
- Aquatic ecosystems (surface waters and wetlands): benthos, pelagic zooplankton and phytoplankton; aquatic vertebrates; food chain effects- consumers of aquatic species (including humans).

Humans

- Sensitive human populations: pregnant woman and developing fetus; infant formula-fed; infant breast-fed exposure to bioaccumulative substances; child; adolescent; elderly; immunocompromised individuals (e.g. asthmatics, allergies, lupus); high fish consumers exposure to bioaccumulative substances.
- Communities with their drinking water intake downstream and in close proximity to STP outfalls.
- Communities with their drinking water sourced from effluent dominated surface waters, particularly during seasonal periods of low flow of freshwater.
- Communities with drinking water sourced from waterways with multiple inputs.
- Rural communities with their drinking water sourced from groundwater in close proximity to areas of intense animal production or land application of sludges.

- Rural communities with private wells in close proximity to septic systems.
- Agricultural workers potential for direct contact with sludges and sludge-amended soils, and exposure to aerosols.
- Consumers of vegetables and fruit grown in liquid-manure and sewage amended soils – there is uncertainy whether uptake of PPCPs in plants occurs.

- **What types of effects are predicted?** *Groups 1 and 2.*

Potential effects that are of concern with respect to PPCPs in the environment include:

- Developmental effects.
- Antibiotic resistance.
- Impairment of reproductive function.
- Multigenerational effects.
- Immunological effects.
- Hormonal effects.
- Incremental effects unknown (as compared to baseline).
- Combined toxicity of low-level mixtures of PPCPs.
- Effects in sensitive human populations (e.g. immuno-compromised individuals).
- Biochemical effects need to be related to health of whole organism and to the ecosystem using a trophic level approach.

Human Health

With respect to human health, workshop participants are unaware of any evidence to date of human health effects related to environmentally low-level exposure to PPCPs. Potential effects, especially to sensitive populations or highly exposed individuals, have not been systematically studied in relation to low-level exposure to PPCPs. Examples of some sensitization reactions are known to occur in certain individuals resulting from direct use of certain drugs (e.g. antibiotics) or personal care products (e.g. hair dyes). Circumstantial evidence of hormonally induced effects in human populations include, reduced sperm counts, early puberty, and endometriosis, but the causal relationship has not be established. The potential for low-level exposure and effects in human populations warrants further investigation.

Ecosystem Health

There is a growing body of evidence of ecosystem effects of certain PPCPs documented by environmental monitoring studies. For example, evidence of bioaccumulation of the fragrances, nitro-musks and polycyclic musks in feral aquatic species ranging from invertebrates to fish has been documented worldwide; however the health significant of these tissue residues is uncertain. Field-monitoring studies in Europe and North America have also documented endocrine disruption effects in fish attributed to exposure to estrogens in the environment. A variety of effects on growth, reproduction and development mediated through the endocrine system have also been reported in a variety of biota, including mollusks, fish and amphibians. Antimicrobial resistance is now recognized worldwide as a major threat to human and animal health. In addition to these

examples of ecosystem effects observations made in the field, results of controlled laboratory studies conducted in non-target aquatic species indicate the ability of certain PPCPs to induce acute effects including lethality, growth inhibition and effects on the reproduction and development.

- **What are the approaches or tests most appropriate for screening or assessing the potential effects?** *Groups 1, 2 and 5.*

Discussions within the three groups emphasized the need for methods that elucidate the effects of chronic low level exposure in non-target species and populations to single chemicals and mixtures of PPCPs. Low level exposure may be defined as concentrations in the range of parts per billion to parts per trillion depending on the type of chemical, its propensity to accumulate in biological tissues and its toxic mechanism of action. It is recognized that PPCPs in use have been assessed by health and environment regulators for the safety of human health in accordance with their intended use. Mammalian toxicology studies of PPCPs typically involve direct short-term exposure using high doses. Workshop participants expressed a need to develop predictive tests to determine the biological activity of these substances and their metabolites and environmental degradation products at environmentally relevant concentrations and above all to determine the significance of biological effects on the whole organism and exposed populations.

One approach that has been used to characterize the aquatic toxicity of complex effluents is the TIE method in which effluents are fractionated on the basis of physical/chemical properties and the various fractions tested for toxicity in an effort to identify the active substances in the mixture. A similar approach may be useful to examine the toxicity of wastewater effluents when done in concert with other analytical chemical and toxicological analysis.

Participants recognize an immediate need to develop a sophisticated screening method to target PPCPs of potential concern from others of lesser concern. Such a screening method would be useful in the assessment of new substances and for the review of substances currently in use to focus future ecosystem, wastewater treatment and drinking water monitoring programs. Accordingly, workshop participants generated the following list of approaches or tests to be considered for development or incorporated into screening tools for assessment of potential effects on human and ecological health:

- *In vitro* assays (e.g. receptor based assays, gene arrays, endocrine endpoints, antibiotic resistance) and the significance to the health of the whole animal, populations and ecosystem.
- Whole effluent toxicity testing and fractionation studies similar to TIE.
- Environmental effects monitoring with comparable baseline studies.
- Ecosystem approach - EU advocates this approach above all other regulatory approaches due to the diverse nature of substances released to surface waters.
- Ecosystem effects – recognize importance to human health.

- Influent and effluent chemical fingerprint (parent chemical, human or animal metabolites and metabolite of activated sludge).
- Toxic mechanism of action.
- Therapeutic mechanism of action or intended therapeutic use.
- Physical-chemical properties.
- Toxic endpoint.
- Dose response.
- Cumulative risks.
- Combined toxicity and analytical chemistry approach.
- Toxicity testing with environmentally relevant exposure scenarios and sensitive indicator species [e.g. daphnia reproduction test, fish early life stage, amphibian (Xenopus) tests, FTEAX, acute toxicity, full life-cycle tests, uterotropic and vitellogenin assays, endocrine tests, antimicrobial resistance studies, gene markers of plasmid mediated resistance].
- Chronic and sub-chronic studies of low levels – what is significance at whole organism and ecosystem level.
- Link to human health using animal models complemented by *in vitro* studies to reduce number of animals.
- Multigenerational studies - to address concern that the deleterious effect (e.g. reproductive system impairment) may not be manifested until adult post generations.
- Animal toxicology extremely important –developmental neurotoxicity can only be done in whole animal (e.g. pyrethroids); cannot replace whole animal testing with *in vitro* studies.
- Genotoxicity and mutagenicity assays.
- Disease surveillance and biomarkers of exposure in human populations. [notable lack of Canadian environmental epidemiology studies].
- Regulatory approach that integrates science health risk with socio-economics, including ethics of animal testing.
- Veterinary product toxicity testing for human and environmental health perspective.
- Animal husbandry and use of veterinary drugs.
- Advances in toxicogenomics; linkages at molecular level.
- Municipal wastewater treatment– no standardized operation procedures.
- Risk/benefit management (e.g. life saving drug are unlikely to be banned therefore the approach needs to focus on waste management procedures to mitigate environmental release).

From a regulatory perspective screening of PPCPs is critical and needs to be linked to research initiatives which will provide necessary knowledge to conduct risk assessments which will enable the development of waste water management options.

9. What are the major research needs? Can you prioritize them in the order to which attention should be given? *All groups.*

The study of PPCPs in the environment and their potential effects on human and ecosystem health is a relatively new area of environmental research. A number of gaps in scientific knowledge of PPCPs in the environment and uncertainties related to environmental loadings and exposure levels are identified in the discussions of the individual groups. Each group presented an overview of perceived major research needs in a plenary session. The following list of perceived major research needs to fill critical gaps in science and understanding of PPCPs in the environment and the potential health effects is a compilation of those put forward by the five groups (This list contributed to the formulation the priorities in the later section).

Major research needs:

- Problem definition – more in depth scoping of issue in a Canadian context.
- Screening framework (criteria) for targeting substances of concern - new substances and other compounds of concern and identification of surrogates for standard toxicity testing and monitoring.
- Characterize PPCPs according to their physical-chemical properties.
- Documentation of human health effects at environmental levels (Lit. Search).
- Baseline data for environmental monitoring.
- Environmental monitoring studies to document presence, levels and effects of PPCPs in Canada.
- Canadian epidemiology studies.
- Biomarkers for human and ecological exposure.
- Biological analysis methods to determine toxic mechanisms of action (e.g. whole animal testing, in vitro systems, soil, water).
- Quantitative Structure Activity Relationships.
- Environmental fate and wastewater treatment degradation studies, including identification of metabolites and breakdown products.
- Volume use data for pharmaceuticals and personal care products (include regional differences).
- Quantify point sources and diffuse sources.
- Predictive (theoretical numerical) models of environmental loadings and environmental fate and food chain models to estimate concentrations in the environment.
- Toxicological studies in appropriate wildlife sentinel species - especially for chronic toxicity, neuroendocrine and developmental effects, multigenerational studies, bioaccumulation, effect of mixtures, mechanism of toxic action. New tools may be needed.
- Information on human and animal metabolites and environmental degradation products and their toxicity.
- Strategy to address potential toxicity of mixtures of low levels of PPCPs in the environment.
- Identification of hormonally active substances in drinking water and food – comprehensive risk assessment.

- Basic understanding of the whole organism health significance of effects at low doses including hormesis across trophic levels.
- Link effects observed in laboratory and field across trophic levels.
- Antibiotic resistance and the significance of environmental routes affecting AMR transmission as it relates to human health. Screening methods for AMR.
- Genetics and molecular understanding.
- Review of Canadian wastewater treatment systems – note regional differences.
- Review of agricultural practices pertaining to storage, treatment and application of manure, sewage sludges and biosolids to soils – note regional differences.
- Study fate of PPCPs in manure, sewage and biosolids applied to agricultural soils *in situ* and mesocosm studies to determine mobility, persistence and ability for uptake by plants.
- Advances in wastewater treatment technologies and agricultural manure treatment and management technologies.
- Advances in disposal technologies and management of waste PPCPs.
- Drinking water analysis to identify presence and levels of substances of concern – provincial and regional basis.
- Human exposure via food – may be less significant than drinking water.
- Identify receiving environments of greatest risk.
- Develop an ecosystem approach focused on the major processes and the functions (e.g. microbial recycling of nutrients).
- Information on ingredients in personal care products.
- International networks for collaboration (e.g. Can., U.S., EU).
- Collaboration among scientists from government, industry and academia.

Priority

As expected due to the complexity of the issue and the diversity of the participants there is not a complete consensus with respect to the prioritization of research needs (see later section on prioritizing research needs). The study of PPCPs in the environment and the potential implications to human and ecological health is in its infancy. Basic research to improve the scientific knowledge and understanding of PPCPs and their metabolites in the environment in terms of their sources, loadings, behaviour, fate, and effects is needed. This understanding will be best achieved through cooperative and collaborative efforts of the international scientific community of government, industry and academia. Overall there is agreement among workshop participants that there is an immediate need for better problem definition of PPCPs and the environmental significance in a Canadian context, and the development of a screening strategy to identify PPCPs of potentially greatest concern.

The objective of Breakout Session II was for participants to review available information on PPCPs in the environment from a regulatory and management perspective to identify knowledge gaps for risk assessment, risk management and regulation development. The assigned questions were designed to lead the group discussions with the ultimate goal of identifying risk assessment, regulatory and management needs.

General Conclusions

- There are many international activities that will influence Canadian scientists, management and regulators in the study and management of PPCPs in the environment (e.g. OECD, VICH, EU, US-GS, US-EPA).
- Substantial data gaps exist in the characterization of exposure and effects of PPCPs in Canada.
- There is sufficient knowledge of the potential concerns of PPCPs in the environment to warrant the development of scientifically based regulations for the protection of human and ecosystem health.
- The potential exposure to PPCPs in humans via drinking water and in Canadian ecosystems via surface water (including the marine environment), groundwater and agricultural soils needs to be determined.
- Current methods are limited for detecting PPCPs at low environmental levels primarily because the methods have not yet been developed for environmental media and the vast number of potential PPCPs and metabolites.
- More information on the physical-chemical properties of individual PPCPs is needed. New and improved environmental fate and exposure models to predict concentrations of PPCPs and their metabolites in the environment are needed.
- There is no standardized municipal wastewater treatment across Canada. To estimate loadings of PPCPs to the environment via municipal STPs a better understanding of the efficacy of various Canadian wastewater treatment technologies in the removal of PPCPs from treated effluents and sludges is needed.
- More information is needed on the potential effects of continual low-level PPCPs exposure in humans and the environment, including effects of mixtures. Empirical knowledge of pharmaceuticals and their therapeutic action in humans does not allow prediction of their ecotoxicity nor of effects of continued low-level exposure in non-target human populations (e.g. early-life-stages, sensitive species, developing fetus, infant, adolescent, immuno-compromised individuals, elderly).
- New and improved analytical techniques and methods for assessment are urgently required.
- Long-term environmental effects monitoring studies and surveillance programs with clear objectives are required for sensitive Canadian watersheds receiving municipal and agricultural-waste and for Canadian drinking water. This will require a collaborative effort of the provinces, territories and federal governments.

- The available data on exposure and effects of PPCPs in the Canadian environment are insufficient to definitively comment on the effectiveness of current risk management options to mitigate potential risks of PPCPs in the environment.
- The vast quantity and wide range of PPCPs demands the development of a prioritization strategy on the basis of grouping substances according to their toxic and or pharmacological activities to facilitate the environmental assessment process.
- There is a need to determine the relevance of conventional NSNR trigger levels for environmental assessment of new substances to PPCPs in the environment, particularly high potency drugs, psychotherapy drugs, hormonally active substances and bioaccumulative substances. New methods and approaches may be required.
- Risk assessment and regulation of PPCPs in the environment may need re-evaluation in concert with the developing science. A periodic review of environmental assessments on an individual product basis or chemical ingredient is suggested with the onus on industry to provide data.
- Risk management options need to be tailored to address issues relevant to PPCPs in the Canadian environment and may include a public education and risk communication strategy, an environmental research strategy, and an agriculture management strategy.
- Scientific-understanding of the issues related to PPCPs in the environment requires a multi-disciplinary approach (e.g. analytical chemistry, microbiology, mammalian and ecotoxicology, field biology, human epidemiology, wastewater and drinking water technology, agriculture). There is both opportunity and need for a collaborative effort in the development of the science (e.g. toxicity tests, analytical methods, data acquisition, field studies) on the part of government, industry and academia.
- A Canadian regulatory approach needs to harmonize with international ones yet remain flexible to address special Canadian needs (e.g. sensitive ecosystems and populations). In addition there is a need for collaborative risk management approaches across three levels of government in Canada and with industry.
    - A number of organizations may provide networking and collaborative opportunities for research and risk management of PPCPs in the environment.

Assessing the Risk

- **Are there activities internationally that will influence Canadians (OECD, U.S., EU harmonization, etc.)? List them.** *Groups 1 and 2.*

There are numerous international activities that will influence Canadians. Some of these include:

- Large scientific studies in the EU (e.g. POSEIDON)
- Monitoring and research studies in the US (e.g. US-GS studies; US EPA Starr Program)
- Harmonization (US FDA – National Environmental Policy Act (NEPA); EU Directive 92/18/EC – EU requirement for assessment of environmental safety; NAFTA.;VICH/EMEA – harmonization group (EU/US/Japan)).

- OECD (e.g. new and improved protocols and testing guidance development / exp assessment / endocrine disruptors/ neurotoxicity).
- International industry associations, workshops and scientific studies (International Water Association, American Water Works Association, Water Environment Federation, etc.)
- Activities of international scientific organizations and societies (Scientific Committee For Cosmetics and Non-Food Products, Society of Environmental Toxicology and Chemistry)
- International agreement and programs (e.g. Biodiversity Convention).

Activities of international organizations (e.g. WHO, integrated risk assessment guidance; UN environmental risk assessment guidance; FAO; Int. Program on Chem. Safety).

- **Is there adequate knowledge and data on exposure and effects to make scientifically sound risk assessments and scientifically defensible regulations in Canada?**
    - **What knowledge/data are needed?**
    - **Are current methods/endpoints adequate? Why?**
    - **Are new methods/approaches and endpoints required? If so what are they?**
    - **Are current approaches adequate for new vs. existing substances?**
    - **In what time frame is it needed?**
    - **Prioritize the research needs for risk assessment and regulation development.**

Groups 1 2 and 5 addressed the above questions from the perspective of exposure and groups 3 and 4 addressed them from the perspective of effects.

Substantial data gaps exist that need to be addressed in order to achieve a sufficient level of confidence in the environmental assessment of PPCPs in Canada. There is sufficient knowledge of the potential concerns of PPCPs in the environment to warrant development of scientifically based regulations for the protection of human and ecosystem health.

Exposure

There are not a lot of data on exposure to PPCPs in the environment but there is enough evidence to raise concern. Additional information is needed to develop risk assessments that go beyond a pathways analysis. Potential exposures via drinking water and surface waters (including the marine environment) and agricultural soils to humans and in Canadian ecosystems need to be determined. Current methods are not adequate to measure exposure of PPCPs at low environmental levels primarily because the methods have not yet been developed for environmental media and the vast number of PPCPs. There is an obvious need to develop analytical methods for the detection of PPCPs in these systems, conduct surveillance programs, and to develop and maintain a database of measured levels of PPCPs in Canadian drinking water, surface waters, ground waters, wastewater effluents and sludges and agricultural soil. Risk assessment and regulatory

approaches need to adopt a low-level indirect exposure approach for PPCPs in the environment. Human health risk assessment methods for food, drugs and cosmetics, pesticides and industrial chemicals are appropriate but may need to be modified to address issues unique to PPCPs in the environment (e.g. hormonal effects).

A key determinant of environmental exposure is the loading rate of PPCPs into the environment. The primary sources of release of PPCPs to the environment are related to their use, excretion and disposal. Canadian data is needed on the volume use of human and veterinary pharmaceuticals, cosmetics and personal care products, and agricultural products used as growth promoters, feed additives, pesticides and in aquaculture. Canadian survey data for PPCPs in effluents of municipal STPs and in wastewater effluents of hospital is needed. Releases of PPCPs could also occur as constituents of manufacturing waste streams. It is suggested that an emissions survey of veterinary drugs, human health drugs and cosmetics and personal care products industries be conducted for Canadian manufacturing facilities.

Another key determinant of environmental exposure is environmental fate including bioaccumulation potential that is governed according to the physical-chemical properties of the introduced substance. Greater information is required on the physical-chemical properties of individual PPCPs. There is a need to improve and develop environmental fate and exposure models to predict concentrations of PPCPs and their metabolites in the environment.

Excreted PPCPs and their metabolites are constituents of wastewater influents. The quantity of PPCPs and their chemical forms released to the environment depends on the type and efficacy of wastewater treatment. There is no standardized municipal wastewater treatment across Canada. To estimate loadings of PPCPs to the environment a better understanding of the efficacy of various Canadian wastewater treatment technologies in the removal of PPCPs from treated effluents and sludges is needed. Participants familiar with large municipal drinking water surveillance programs and wastewater treatment in Canada expressed a greater level-of-concern for those systems operating with primary and secondary treatment only, and for septic-based systems.

There is a notable lack of information on metabolites of PPCPs and their excretion rates in humans and animals. Similarly there is a lack of data on the environmental degradation products of PPCPs, including transformation products formed in wastewater STPs. These need to be identified and characterized with respect to their physical-chemical properties and environmental fate.

There is a need to review current regulations for storage, treatment, application and disposal of animal manures, particularly those pertaining to large industrial farms, race-horse facilities and animal health practices from an exposure pathways analysis perspective for PPCPs in the environment.

Information on the volume use of cosmetics and personal care products in Canada is required keeping in mind that the majority of rinse-off products enter municipal STPs.

Effects

More information is need on the potential effects of continual low-level exposure of humans and the environment to PPCPs. Empirical knowledge of pharmaceuticals and their therapeutic action in humans does not allow prediction of ecotoxicity. The toxic effect may be different than the therapeutic effect for many drugs. More information is needed on the toxic mechanism of action, receptor-mediated effects and the significance to whole organism health. Therefore new information on the ecotoxicity of low levels of PPCPs is required. Validation of conventional acute to chronic ratios needs to be conducted to determine their applicability to PPCPs in the environment. Some neuroendocrine-disrupting substances have been found to induce effects only in the F1 generation; thus multigenerational studies may be required to assess the potential health effects of certain PPCPs. Physical-chemical properties and fate data for individual PPCPs can be useful in identifying appropriate environmental exposure pathways to study.

Concern is expressed that current health and environmental assessment approaches may not be adequate to assess the potential human health and environmental effects for new and existing PPCPs. This is because for existing chemicals there is limited or no historical data on chronic effects of low level exposures, effects of combined exposures, and ecological effects in sensitive non-target organisms and sensitive life stages for ecologically relevant endpoints. To conduct environmental assessments these data are required for PPCPs in standard test species representative of all trophic levels. A battery of tests-approach to cover a range of biological endpoints specific to the toxic mechanism of action of the PPCPs is required. Ecosystem studies (mesocosm or field studies) need to target key ecosystem components and processes. Environmental assessment approaches need to be modified to address issues related to the development and transfer of antimicrobial resistance and its significance to human and animal health. PMRA guidelines for environmental assessment of pesticides in Canada include both a human and an ecological component to assess the potential health effects in non-target species. This approach may be adaptable to the environmental assessment of PPCPs. Given the vast quantity and wide range of PPCPs a strategy for grouping substances according to their toxic and or pharmacological activities is needed to facilitate the environmental assessment process. Conventional NSNR trigger levels for the environmental assessment of new substances may not be appropriate for certain PPCPs, particularly high potency drugs, psychotherapy drugs and hormonally active substances.

Risk assessments need to integrate results of whole effluent toxicity testing with results of field monitoring studies. Comprehensive data sets are currently not available for PPCPs in the environment. Furthermore, in order to assess the potential for food chain related effects a better understanding is needed of the bioaccumulation potential of certain PPCPS in aquatic species and food producing animals, as well as uptake in plants. Uptake of PPCPs in plants was considered to be of a lesser priority as compared with all other identified research needs.

What time frame is needed?

The timeframe for new and improved methods for assessment and analytical techniques is immediate. Regulatory and risk assessment approaches for Canada need to be developed in harmonization with international approaches. This will allow industry to provide necessary data to countries within a similar timeframe. Regulations for environmental assessment need an element of flexibility in order to address situations and substances with extraordinary circumstances. In Canada existing PPCPs must be categorized by August 2006 (in 4.5 years). Thus there is an immediate need for screening tools to group and prioritize PPCPs for environmental assessment. The time frame for assessment of new industrial chemicals under CEPA Schedule 3 substances is 45 days and for Schedule 1 substance is 5 days. New tools are urgently needed to facilitate these assessments.

Research needs

The following research needs for risk assessment and regulation development were identified:

- Screening of PPCPs based on use, fate and toxic potency.
- Better understanding of the low level chronic toxicity of PPCPs in non-target species including humans.
- Are standard environmental assessment trigger levels adequate to assess potential developmental and multigenerational effects?
- Development of standard tests for chemical classes of concern.
- Alternative to LC_{50} – possibilities: cell assays (liver, endocrine disruptors); antibiotic resistance; genotoxicity; shortened life-cycle tests; low dose test for growth, reproduction and survival.
- Strategic environmental monitoring to determine exposure and effects.
- Screening of whole effluents based on potency of mixtures in wastewater and drinking water.
- Understanding of sources and their contribution to environmental loadings.
- Research to improve wastewater technologies to remove substances of concern.
- Research emphasis on antimicrobial resistance and endocrine disrupting substances in the environment.
- Development of QSARs to predict toxicity.

Managing the Risk

- **Are monitoring programs needed? If so what needs to be included?**
  All groups addressed this question.

Monitoring programs are urgently required. This will require a collaborative effort of the provinces, territories and federal governments. Before PPCPs monitoring programs are initiated robust analyses on a regional basis of volume use data for pharmaceuticals, natural health products and cosmetics and personal care products is essential to focus on priority substances. Environmental effects monitoring studies and surveillance programs

with clear objectives are required. Long-term monitoring studies need to be conducted that are statistically meaningful in order to observe temporal trends in data. A single snapshot approach should be avoided. Applied methodologies and procedures must ensure good QA/QC.

The following monitoring programs are needed to assess PPCPs in the Canadian environment:

- Surveillance of PPCPs (types and concentration) in groundwater, drinking water and surface waters.
- National fate and effects monitoring of agricultural ecosystems to determine mobility of PPCPs in manures, applied sewage sludge and biosolids, soils and ground water.
- Environmental antimicrobial resistance surveys to determine development, transfer and health significance.
- Ecosystem fate and effects monitoring of aquaculture.
- Continuation and expansion of in-place Canadian environmental monitoring programs, including baseline studies to provide a reference for comparison.
- Biological monitoring for indicators of exposure and health effects in sensitive Canadian ecosystems.
- National municipal wastewater influent and effluent survey cross-referenced to treatment technologies and basic operating conditions.
- Survey of PPCPs in hospital wastewater effluents.
- Comprehensive watershed analysis for sensitive Canadian aquatic ecosystems.
- Canadian disease surveillance studies.

- **Can the effectiveness of current or proposed regulations be assessed or monitored?** *Groups 1, 2 and 5.*

The effectiveness of current or proposed regulations can be assessed and monitored. To evaluate the effectiveness of current or proposed regulations requires clearly identified performance indicators of success of the regulations are needed. Since the sciences of human and eco- toxicology, analytical chemistry, and new product development are dynamic processes, current or proposed regulations may need to be modified to meet developing needs. With respect to PPCPs in the environment for which there is a lack of hazard information there may be a need to re-evaluate regulations in concert with the developing science. Workshop participants note that guidelines and regulations under CEPA need to be flexible to allow for extraordinary circumstances. A periodic review of environmental assessments on an individual product basis or chemical ingredient is suggested as a mean of achieving this. For example a five year review period to revisit regulatory decisions with respect to tier level and with an onus on industry to provide data to regulators. This approach is similar to that used in the UK for environmental assessment of veterinary drugs.

- **How effective are current risk management options: municipal treatment, Best-management practices for agriculture, drinking water treatment?** *Groups 1, 3 and 4.*
- **Can/should risk management options be developed and what research is needed?** *Groups 1, 3 and 4.*

The responses to questions 5 and 6 are combined below.

It is generally accepted that the available data on exposure and effects of PPCPs in the Canadian environment are insufficient to definitively comment on the effectiveness of current risk management options to mitigate potential risks of PPCPs in the environment. In order to better answer this question certain information is required that is in general applicable to agriculture, wastewater treatment, drinking water treatment and pharmaceutical use and disposal and other practices. These include:

- the development of appropriate guidelines and environmental stewardship programs,
- evaluation of current operational tools,
- comparative review of management options with respect to their suitability for PPCPs,
- identification of uncertainties in risk management options and an ability to meet the site-specific needs or regional needs.

In addition, there is a need to know whether good management practices are being implemented across Canada by both large operations and small cottage industries or family farms. Finally better source control is a recognized key to the mitigation of the release of PPCPs into the Canadian environment. This may be partially accomplished through an effective education and risk communication strategy that targets the Canadian consumer, physicians and health care professionals, veterinarians, agriculture and aquaculture industry, pharmaceutical industry, personal care and cosmetics industry and natural health products industry.

There are numerous question and needs related to the risk management of PPCPs in the Canadian environment. Some of these include:

Municipal wastewater treatment

- What are the PPCPS of concern?
- What is their ionic form?
- What are the removal rates for PPCPs?
- Are current WWTP operation conditions suitable for substances of concern?
- How can these be improved?
- What options are available for removal of PPCPs in WWTPs?
- Need for a life-cycle assessment of products.
- Need to develop and implement use of models to project WWTP loadings and concentrations in watershed.

Agriculture

- What manure management disposal options are available to the large and small production facilities?

- Need to evaluate the effectiveness of odour and nutrient control measures under current agricultural Best Management Practices for manure, sewage, biosolids disposal via spreading on agricultural land to determine whether they are protective for PPCPs.
- What are most appropriate to mitigate the release of PPCPs in the agricultural environment?
- Are these being implemented across Canada; regionally?
- Need for information on the mobility, persistence and effect of PPCPs in agricultural soils?
- Need to determine on a site-specific basis the potential for PPCPs to leach to groundwater or enter surface waters via agricultural runoff.

Drinking water

- What PPCPs are present in Canadian drinking water?
- At what levels?
- What good management options available for drinking water (e.g. activated carbon filtration).
- What is their effectiveness for the removal of PPCPs?

Pharmaceuticals use and disposal practices

- Need for prevention of over-prescription and inappropriate use requires communication with physicians.
- Need for environmental stewardship programs such as those being implemented in western provinces to keep unused pharmaceutical products out of landfills and sewers through industry supported collection programs via local pharmacies. Similar disposal management programs are being developed for Ontario and the eastern provinces.

Risk management options need to be developed that are tailored to address issues relevant to PPCPs in the Canadian environment. These could include a public education and risk communication strategy, environmental research strategy, National wastewater treatment, and agriculture management strategy.

- **What actions need to be taken in the short-term and the long-term to reduce exposure and potential risks?** *Groups 2, 4 and 5.*

Short-term solutions:

- Risk communication of potential for environmental effects of PPCPs to encourage more environmentally conscious use and disposal practices.
- Focus education efforts to reduce unnecessary use of antibiotics and other drugs and PPCPS in humans, food producing animals, and other animals.
- Develop and implement collection and disposal programs for unused drugs (prescription and OTCs).
- Develop and implement hospital waste management programs.

Long-term solutions:

- Development and implement agricultural Best Management Practices for large animal production facilities and small farms.
- Drinking water survey of PPCPs, development and implementation of removal technologies.
- Municipal wastewater survey, modifications to incorporate new PPCPs removal technologies or approaches, including control of storm water bypasses.
- Development and implementation of Best Management Practices for aquaculture.

- **Are there opportunities for collaboration among various research groups?** *All groups.*

There are numerous opportunities for collaboration. Scientific-understanding of the issues related to PPCPs in the environment requires a multi-disciplinary approach (e.g. analytical chemistry, microbiology, mammalian and ecotoxicology, field biology, human epidemiology, wastewater and drinking water technology, agriculture). There is both opportunity and need for a collaborative effort in:

- The development of test procedures and analytical methods.
- Data acquisition.
- The harmonization of international regulatory approach with flexibility to address special Canadian needs (e.g. sensitive ecosystems such as the Artic, Bay of Fundy, and aboriginal communities).
- Collaborative risk management approaches across three levels of government in Canada and with industry.
- Environmental monitoring and surveillance programs in Canada.

Workshops, such as this one, provide an excellent opportunity for the exchange of scientific information, experiences and ideas, as well as the opportunity to develop cooperative and collaborative networks and associations for future research and management initiatives. The success of these activities requires the support of all three levels of Canadian government, industry, academia and NGOs.

- **Prioritize the research needs for risk management.** *All groups.*

Research needs

The following is a list of research needs for the risk management of PPCPs in the Canadian environment:

- Characterize the Canadian situation with respect to PPCPs volume use, wastewater treatment and agricultural practices, receiving environment and sensitive populations.
- More information on veterinary drug use (e.g. antibiotics; bovine growth hormone).
- Prioritize PPCPs of concern to human health and ecological health and include consideration of potential interactive low-level effects.
- Identify surrogate chemicals and sentinel species for biological effects monitoring and testing.

- Maintain comprehensive databases with relevant information on PPCPs, including chemical name, CAS no., use, properties, fate and toxicity data, and monitoring data. Information will be of use in identification of priority substances and surrogates.
- Determine the suitability of current trigger values in the New Substances Notification Regulations for the environmental assessment of PPCPs in the environment.
- Better define potential risk: fill data gaps in exposure assessment and hazard assessment.

  Hazard:
  - Identify toxic mechanism of action for PPCPs and compare to therapeutic mechanism; be aware that pharmaceuticals work in humans based on empirical knowledge often the therapeutic mechanism is unknown - can't predict in ecological species.
  - Validate test methods of PPCPs and acute to chronic ratios; determine the relevance of toxic endpoints; are they applicable to PPCPs?
  - Toxicity of PPCPs and metabolites low level exposures (ppb to ppt) recognizing that the therapeutic action of drugs in humans is not always same as their toxicity or effects in non-target species.
  - Toxicity of mixtures of PPCPs and metabolites at low levels.
  - Receptor mediated mechanisms and their relevance to health and survival of whole organism and populations.
  - Develop battery of tests for classes of PPCPs of concern.

  Exposure:
  - Influence of site-specific characteristic of water treatment systems and receiving environment on exposure.
  - Identification of metabolites of PPCPs.
  - Fate and bioaccumulation potentials of PPCPs, metabolites and degradation products in wastewater treatment systems, manure- holding tanks, sewage-sludge bioreactors, surface waters, groundwater and soils.
  - Validate methods and models for estimation of exposure to PPCPs in the environment.
- Ranking of wastewater treatment technologies with respect to PPCPs removal efficiencies.
- Expand current drinking water surveillance for PPCPs such as antibiotics, cardiac drugs, psychotherapy drugs, fertility drugs and other steroids.
- Develop fate and exposure models for PPCPs.
- Site-specific watershed studies of inputs of PPCPs through known sources (e.g. wastewater STP effluents and agricultural runoff) and monitoring studies to calibrate fate and exposure models of PPCPs for use in the determination of environmental concentrations of PPCPs.
- Surveillance of rural communities with septic-based sewage systems and groundwater supplies for drinking water.

- Surveillance of agricultural practices for the management of animal wastes and the presence of PPCPs in the ambient environment.
- Surveillance of agricultural practices of land-application of sewage, liquid manure and biosolids and the presence of PPCPs in the ambient environment.
- Surveillance of aquaculture practices involving the use and disposal of PPCPs and their presence in the surrounding environment (focus on sensitive ecosystems).
- Field studies: environmental monitoring of indigenous species; exposure effects in naïve species.
- Maintain an inventory of activities internationally being conducted on PPCPs; establish a website dedicated to up dating current events.

Other Points Raised in Breakout Groups:

Workshop participants promote TSRI as a successful working example of a program that facilitates a cooperative funding, research and management approach by government, industry and academia.

Health Canada has no legislative authority under F&DA to remove products from the market on the basis of potential or actual environmental toxicity or adverse ecosystem health effects.

How will existing substances on DSL, and ingredients in health and personal care products currently in use be assessed? Concern is expressed regarding the possible difficulty in obtaining historical data.

Dilution rate is a key determinant of environmental concentrations but is not a solution to pollution; potential for cumulative effects must be considered.

Prioritization of Research Needs and Path Forward

Summary of Research Needs and Prioritization

Mark Servos and Elizabeth Innes, Session Co-chairs

One of the primary objectives of the workshop was to identify major science research needs for risk assessment, management and regulation in relation to PPCPs in the Canadian environment. Research needs were identified through the course of discussions in each breakout group and these were presented to the workshop-at-large in summary/plenary sessions. The research needs identified by the groups in plenary and written reports were synthesized by the organizing committee into a list of major research needs. These were presented to the workshop participants on the final day for voting with respect to priority. Each participant was given ten adhesive dots and asked to place them on what they perceived to be the highest priorities; a maximum of three dots could be applied to any one research need. It is recognized that there are limitations to this approach but the results are a general indication of the highest priorities.

The research needs identified fell into several major categories:

Exposure

- Prioritize/screening PPCPs of concern (volumes, loadings, pathways, bioaccumulation).
- Develop models to predict loading, fate and exposure.
- Developing chemical and biological analytical methods for assessing exposure of PPCPs.
- Evaluating environmental exposure from agriculture (e.g. biosolids application).
- Evaluating environmental exposure from wastewater (e.g. STPs)
- Evaluating environmental exposure from aquaculture (e.g. use of antiparasiticides).
- Evaluating human exposure from drinking water (sensitive groups, the elderly, children, etc.).

Effects

- Developing environmental effects assays (acute, chronic, life-cycle) at appropriate trophic levels.
- Evaluating/developing human health effects assays (high dose vs. low dose)
- Improved fundamental understanding of mode of action and pharmacokinetics of PPCPs in humans and non-target species.
- Evaluating environmental antimicrobial resistance and response to PPCPs.
- Assessment of environmental effects including baseline studies (i.e. EEM approach)
- Better understanding of effects of mixtures (e.g. STP whole effluents, TIE approach).
- Develop/validate predictive tools (e.g. models, QSARs).
- Determine relevance of current assessment methods.

- Development and validation of appropriate methods for assessing effects of PPCPs (harmonization with OECD, US-EPA test development).
- Human disease/health surveillance (e.g. antimicrobial resistance, neurological and behavioural development).

Managing Risk

- Developing practices to reduce the use of PPCPs of concern (e.g. IPM-approach for treating sea lice, developing 'greener' drugs).
- Devising methods and technologies for treating wastes (municipal, agriculture) to reduce the release of PPCPs.
- Developing best management practices for land application of animal and municipal wastes.

Results of Voting

The outcome of workshop participant voting is presented in Table 2.

Table 2. Research priorities identified during a multi-stakeholder workshop, "Assessment and Management of Pharmaceuticals and Personal Care Products in the Canadian Environment", Niagara-on-the-Lake, Ontario, Feb. 24-27, 2002.

Rank	Research Priorities for Pharmaceuticals and Personal Care Products	Votes
1.	Devising methods and technologies for treating wastes (municipal, agricultural) to reduce the release of PPCPs.	57
2.	Evaluating human exposure from drinking water (sensitive groups, the elderly, children, etc.).	54
3.	Developing environmental effects assays (acute, chronic, life-cycle) at appropriate trophic levels.	54
4.	Developing best management practices for land application of animal and municipal wastes.	51
5.	Developing chemical and biological analytical methods for assessing exposure of PPCPs.	46
6.	Developing practices to reduce the use of PPCPs of concern (e.g. best management practices).	46
7.	Developing models to predict loading, fate and exposure.	43
8.	Evaluating environmental exposure from wastewater (e.g. Sewage Treatment Plants).	42
9.	Assessment of environmental effects including baseline studies (e.g. Environmental Effects Monitoring Program approach).	40
10.	Prioritization of PPCPs of concern (volumes, loadings, pathways, bioaccumulation).	34
11.	Better understanding of effects of mixtures (e.g. STP whole effluents, Toxicity Identification Evaluation approach).	32

Rank	Research Priorities for Pharmaceuticals and Personal Care Products	Votes
12.	Development and validation of appropriate methods for assessing effects of PPCPs (harmonization with OECD, US-EPA test development).	30
13.	Improved fundamental understanding of mode of action and pharmacokinetics of PPCPs in humans and non-target species.	29
14.	Evaluating environmental antimicrobial resistance and response to PPCPs.	28
15.	Evaluating and developing human health effects assays (high dose vs. low dose).	27
16.	Human disease and human health surveillance (e.g. antimicrobial resistance, neurological and behavioral development).	21
17.	Evaluating environmental exposure from agriculture (e.g. manure, biosolids application).	19
18.	Developing and validating predictive tools (e.g. models, Quantitative Structure Activity Relationships).	19
19.	Determine relevance of current assessment methods	18
20.	Evaluating environmental exposure from aquaculture (e.g. use of antiparasiticides).	7

The Path Forward

Science-policy linkages are an important part of formulating the necessary background for addressing emerging issues such as PPCPs in the environment. Round Table discussion groups were used on the last morning as a way to change the mix of participants and facilitate discussion of the path forward. Each table was charged with the task to:

- Identify the major drivers affecting the progress of science research and risk management of PPCPs in the environment?
- Identify the major actions or activities that are needed to fill scientific data gaps?
- Identify the major barriers to the progress of science research and risk management of PPCPs in the environment?

Groups were given approximately 15 minutes to discuss each question and record their answers, then the groups were given the opportunity to share their answers/ideas with other participants though a mediated discussion. The responses were recorded and are summarized below.

Results of Round-Table Discussions

Question 1: **What will be the major drivers that will influence the progress of the science, regulation and policy related to this issue in Canada (e.g. CEPA/FD&A,**

international activities etc.)? *The first three perceived drivers are ranked high and of immediate concern.*

- Public awareness, concern and media attention (*Immediate*).
- Legislation and regulations (e.g. CEPA, F&DA, FA, AHA) (*Immediate*).
- New scientific evidence; need to address scientific uncertainty (*Immediate*).
- Government and industry liability.
- Political will.
- International initiatives, harmonization and trade.
- Required 5 year review of CEPA.
- Changing Canadian demographics.
- Existing scientific expertise and technology.
- Commitment to a National Wastewater Strategy.
- Precautionary principle in face of uncertainty to human and environmental health.

Question 2: What activities/actions are required to move this issue forward in a Canadian context (e.g. specific meetings/workshops, public communication, etc.)? *The three most urgent actions are noted below and others identified with their relative urgency (H,M,L).*

- Complete the problem definition (e.g. international research inventory; identify Canadian priorities) (*Immediate, High*).
- Determine PPCPs use and loadings to the Canadian environment (*Immediate, High*).
- Develop and implement a national research strategy; i.e. research on exposure, effects, risk management (*Immediate, High*).
- Develop surveillance and monitoring programs (human and environmental health) (*High*).
- Establish stable and long-term funding and resources (e.g. A-Base, TSRI, etc.) (*High*).
- Facilitate risk communication and education (public, all levels of government and industry) (*High*).
- Establish scientific networks and collaborative efforts nationally and internationally (e.g. workshops, existing organizations like SETAC) (*High*).
- Collaboration and cooperation among all levels of government (*High*).
- Review and develop regulations (*Medium*).
- Integrate PPCP strategy within existing national and international programs (e.g. National Wastewater Strategy, VICH, ICH) (*Medium*).
- Collaboration and cooperation among stakeholders (*Medium*).
- Facilitate science-policy interaction.
- Dialogue among key federal Departments regarding Best Management Practices (*Medium*).
- Dialogue with human and animal health care professionals regarding use and disposal (*Medium*).

Question 3: What barriers may prevent making progress on addressing this issue in

Canada; are there solutions?

- Complexity of issue and lack of Canadian data/understanding.
- Limited resources, infrastructure and funding; lack of secure sustainable funding and commitment.
- Potential economic impacts for consumers and industry.
- Limitations of current technologies and methodologies.
- Competing environmental priorities.
- Lack of a coherent strategy.
- Lack of cooperation and communications among and across Departments and levels of government.
- Access to proprietary information on specific PPCPs.

In addition to the above, a number of issues not specifically dealt with in the workshop but worthy of attention were identified: the fate of PPCPs in sewage treatment plants; physical-chemical properties of PPCPs; industry perspectives on this issue; an overview of PPCP industries (e.g. magnitude of products and types in use); hospitals current waste treatment practices; risk benefit analysis of PPCPs; socio-economics of the issue; and behavioral change and risk communication within the public, industry and all levels of government.

Conclusions and Recommendations of the Workshop

Recent studies in Europe and the United States have documented the presence of a wide variety of pharmaceuticals and personal care products (PPCPs) in the environment. However, there are few data are available to characterize the sources, exposure and effects of PPCPs within the Canadian environment. Municipal sewage, agricultural and aquaculture wastes have been identified as sources of PPCPs such as antibiotics, blood lipid regulators, analgesics, anti-inflammatories, anti-epileptics, natural and synthetic hormones, fragrances (musks), nonylphenol ethoxylates, disinfectants and anti-parasiticides. Many of these substances are designed to target specific biological functions at therapeutic doses. There is mounting evidence that some of these chemicals have the potential to induce adverse health effects in non-target species and possibly humans when exposed to low levels. Effects of concern include disruption of development and reproduction in exposed individuals and their offspring, as well as the enhancement of antibiotic resistant bacteria. There is great uncertainty what the potential long-term human health and ecological health consequences may be resulting from continuous low-level exposure to these substances, especially in sensitive life stages and populations. Release of PPCPs into the environment will continue, and will diversify with new product developments dependent upon changing use patterns in humans and animal production. New PPCPs, especially drugs, are likely to be engineered to be increasingly persistent in the body, specific and biologically active.

Major Conclusions of the Scientific Workshop

There is a need:

- to clearly define the scope of the issue within a Canadian context;
- to immediately obtain scientific data on exposure and effects of PPCPs in the Canadian environment;
- to collaborate internationally across sectors to address knowledge gaps and reduce scientific uncertainty;
- for an interdisciplinary, multi-sector approach to support development of a Canadian regulatory framework in harmonization with international organizations (e.g. VICH, OECD);
- to implement a comprehensive national science program to address risk assessment and risk management of PPCPs in the Canadian environment;
- for the development and implementation of "best management practices" and risk management options; and
- for a national communication strategy.

Recommendations for the Implementation of a National Science Agenda

- Create a multidisciplinary research initiative in cooperation with all levels of government, industry and academia.

- Prioritize concerns by reviewing existing information to identify sources, distribution, and use patterns of PPCPs, their likely environmental fate, potency, mechanism of action, and assessment methods.
- Design and implement a data collection program for assessing exposure to PPCPs in Canada (wastewater, drinking water, groundwater, surface water and agricultural soils).
- Establish a network within the international scientific community to promote the exchange of scientific information to minimize duplication of effort and capitalize on existing expertise and programs.
- Contribute to the international programs for test development and validation and integrate international standardized tests within the Canadian regulatory framework.
- Engage other levels of government to address agricultural practices, wastewater technology, and drinking water quality across the nation.
- Implement a risk communication strategy to educate industry, government and public stakeholders on appropriate use, disposal and management practices for PPCPs.

Background Information

This is a listing of some relevant literature on pharmaceuticals and personal care products in the environment. It is a short list of some key scientific articles, reviews documents and books.

Committee for Proprietary Medicinal Products (CPMP). 2001. Discussion paper on environmental risk assessment of non-genetically modified organism (Non-GMO) containing medicinal products for human use. January 25, 2001. The European Agency for the Evaluation of Medicinal Products Evaluation of Medicines for Human Use. CPMP/SWP/4447/00 http://www.emea.eu.int/htms/human/swp/swpdisj.htm

Committee for Veterinary Medicinal Products. 1998. Note for Guidance: Environmental Risk Assessment for Veterinary Medicinal Products Other Than GMO-Containing and Immunololical products. Committee for Veterinary Medicinal Products. Final Approval by the CVMP 14-16-January 1997. January, 1998. EMEA/CVMP/055/96-FINAL. http://vich.eudra.org/pdf/2000/Gl06_st7.pdf

Council of Great Lakes Research Managers. 2001. Emerging contaminants and pharmaceuticals in Great Lakes waters. In: Priorities 1999~2001. Priorities and Progress under the Great Lakes Water Quality Agreement. The Council of Great Lakes Research Managers Report to the IJC. Sept. 2001. ISBN 1-894280-27-X. http://www.ijc.org/boards/cglr/pr9901/index.html

Daughton, C.G. and Jones-Lepp, T. (eds.). 2001. Pharmaceuticals and Personal Care Products in the Environment: Scientific and Regulatory Issues, *Symposium Series 791*; American Chemical Society: Washington, D.C. http://www.epa.gov/esd/chemistry/pharma/book.htm

Daughton, C.G. and T.A. Ternes. 1999. Phamaceuticals and Personal Care Products in the Environment: Agents of subtle change? Environmental Health Perspectives. 107:907-938. http://www.epa.gov/nerlesd1/chemistry/ppcp/images/errata.pdf

Environment Canada. 2001. The state of municipal wastewater effluents in Canada. Indicators and Assessment Office. Ecosystem Directorate. Environmental Conservation Service. Environment Canada. 2001. http://www.ec.gc.ca/soer-ree/english/national/MWWE.pdf

Giger, W. 1999. Emerging Chemical drinking water contaminants. In: Identifying Future Drinking Water Contaminants, National Academy Press, Washington DC. http://www.nap.edu/books/0309064325/html/

Hileman, B. 2001. Troubled Waters, EPA, USGS try to quantify prevalence, risks of compounds from drugs, personal care products. Chemical and Engineering News. Dec.3, 2001:31-33.

Jorgensen, S.E. and B Halling-Sorenson. Drugs in the environment. Chemosphere 40:691-699.

Kaiser K. and S.P. Niculescu. 2001. On the PNN Modeling of estrogen receptor binding data for carboxylic acid esters and organochlorine compounds. Water Qual Res. J. Canada. 36:619-630.

Kolpin, D.W., E.T. Furlong, M.T. Meyer, E.M. Thurman, S.D. Zaugg, L.B. Barber, and HT. Buxton. 2002. Pharmaceuticals, Hormones, and Other Organic Wastewater Contaminants in U.S. Streams, 1999-2000: A National Reconnaissance. Environmental Science and Technology 36:1202-1211.
http://pubs.acs.org/hotartcl/est/es011055j_rev.html

Kümmerer, K. (ed.) 2001. Pharmaceuticals in the Environment: Source, fate, effects and risks. Springer, Heidelberg. 265 p.

Metcalfe, C., B. Koenig and X-S. Miao, T. Ternes, and J. Struger. 2002. Prescription and Non-Prescription Drugs in the Canadian Aquatic Environment. Draft prepared for EC/HC Workshop, Assessment and Management of Pharmaceuticals and Personal Care Products in the Canadian Environment, Niagara-on-the-Lake, Ont., Feb. 24-27, 2002.

Scientific Committee on Toxicology, Ecotoxicity and the Environment (CSTEE). 2001. Opinion on: Draft CPMP Discussion Paper on Environmental Risk Assessment of Scientific Committee on Toxicity, Ecotoxicity and the Environment (CSTEE). Medicinal Products for Human Use [Non-Genetically Modified Organism (Non-GMO) Containing] Scientific Committee on Toxicity, Ecotoxicity and the Environment (CSTEE). Brussels, 12 June 2001. C2/JCD/csteeop/CPMPpaperRAssessHumPharm12062001/D(01).

Sedlak, D., J. Gray, K. Pinkston. 2000. Understanding Micro-Contaminants in Recycled Water. Environmental Science & Technology News, Dec., 2000:508-515.

Servos, M., P. Chambers, R. MacDonald and G. Van Der Kraak. 2002. Municipal Wastewater Effluents. In: Environment Canada. Threats to Sources of Drinking Water and Aquatic Ecosystem Health in Canada. National Water Research Institute, Burlington, Ontario. NWRI Scientific Assessment Report Series no.1. 72 p. http://www.cciw.ca/nwri/threats/intro-e.html

Servos, M.R. and E. Innes. 2001. Towards a research strategy on assessment of human and agricultural pharmaceuticals and therapeutic products in the Canadian environment. National Water Research Institute, Environment Canada. NWRI Contribution No.01-054.

Servos, M.R., D.T. Bennie, M.E. Starodub and J.C. Orr. 2002. Pharmaceuticals and personal care products in the environment: A summary of published literature. National Water Research Institute, Environment Canada. NWRI Contribution No. 02-309.

Stuer-Laridsen, F. M. Birkved, L.P. Hansen, H-C Holten Lutzhoft and B. Halling-Sorensen. Environmental risk assessment of human pharmaceuticals in Denmark after normal therapeutic use. Chemosphere 40:783-793.

Ternes, T.A., M. Stumpf, J. Mueller, K. Haberer, R-D. Wilken and M. Servos. 1999. Behavior and occurrence of estrogens in municipal sewage treatment plants – I. Investigations in Germany, Canada, and Brazil. Sci. Total Environment 225:81-90.

US FDA. Guidance for Industry. Environmental Assessment of Human Drug and Biologics Applications. U.S. Dept. of health and Human Services, Food and Drug Administration. Center for Drug Evaluation and research (CDER). Center for Biologics Evaluation and Research (CBER). July 1998. CMC 6. Revision 1.
http://www.fda.gov/cder/guidance/1730fnl.pdf

Related Websites and Links

Health Canada
http://www.hc-sc.gc.ca/
Environmental Assessment Regulations; Food and Drug Products and the Environment
http://www.hc-sc.gc.ca/ear-ree/noi_e.html

Environment Canada
http://www.ec.gc.ca/
New Substances
http://www.ec.gc.ca/substances/nsb/eng/index_e.htm
National Water Research Institute
http://www.nwri.ca

Agriculture and Agri-Food Canada
http://www.agr.gc.ca/

Canadian Food Inspection Agency
http://www.inspection.gc.ca/

Department of Fisheries and Oceans Canada
http://www.ncr.dfo.ca/index.htm

Organization for Economic Co-operation and Development (OECD)
http://www.oecd.org

European Agency for the Evaluation of Medicinal Products
http://www.emea.eu.int/home.htm

International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Products (VICH)
http://vich.eudra.org/

US Environmental Protection Agency
EPA FIFRA Ecological Risk Assessment Page
http://www.epa.gov/oppefed1/ecorisk/index.htm
EPA ORD National Center for Environmental Assessment
http://www.epa.gov/ncea/document.htm
Pharmaceuticals in the Environment
http://www.epa.gov/nerlesd1/chemistry/pharma/index.htm

US Geological Survey
http://toxics.usgs.gov/regional/emc.html

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