



October 2014



PRESCRIPTION PHARMACEUTICALS IN CANADA

Unintended Consequences

Standing Senate Committee on
Social Affairs, Science and Technology

The Honourable Kelvin K. Ogilvie, *Chair*

The Honourable Art Eggleton, P.C., *Deputy Chair*





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ORDER OF REFERENCE

Extract from the *Journals of the Senate* of Tuesday, November 19, 2013:

The Honourable Senator Ogilvie moved, seconded by the Honourable Senator Runciman:

That the Standing Senate Committee on Social Affairs, Science and Technology be authorized to examine and report on prescription pharmaceuticals in Canada, including but not limited to:

- (a) the process to approve prescription pharmaceuticals with a particular focus on clinical trials;*
- (b) the post-approval monitoring of prescription pharmaceuticals;*
- (c) the off-label use of prescription pharmaceuticals; and*
- (d) the nature of unintended consequences in the use of prescription pharmaceuticals.*

That the papers and evidence received and taken and work accomplished by the committee on this subject during the First Session of the Forty-first Parliament be referred to the committee; and

That the committee submit its final report no later than December 31, 2014 and that the committee retain until March 31, 2015, all powers necessary to publicize its findings.

After debate,

The question being put on the motion, it was adopted.

Gary W. O'Brien
Clerk of the Senate

MEMBERS

The Honourable Kelvin Kenneth Ogilvie, *Chair*
The Honourable Art Eggleton, P.C., *Deputy Chair*

The Honourable Senators:

Maria Chaput, Jane Cordy, Nicole Eaton, Tobias Enverga, Jim Munson, Nancy Ruth, Hugh Segal, Judith Seidman, Asha Seth, Carolyn Stewart Olsen.

Ex Officio Members:

The Honourable Senators Claude Carignan, P.C. (or Yonah Martin) and James Cowan (or Claudette Tardif).

Other Senators who have participated from time to time in the study:

The Honourable Senators Bellemare, Beyak, Doyle, Lang, Maltais, Moore, Rivard and Tannas.

Parliamentary Information and Research Services, Library of Parliament:

Sonya Norris, Analyst.

Clerk of the Committee:

Jessica Richardson.

Senate Committees Directorate:

Diane McMartin, Administrative Assistant.



TABLE OF CONTENTS

ORDER OF REFERENCE	1
MEMBERS	1
INTRODUCTION	2
CONTEXT	3
UNINTENDED, BUT NOT UNEXPECTED, ISSUES OF CONCERN	4
Abuse, Misuse and Addiction	4
Antibiotic Resistance	7
Counterfeit and Substandard Drugs	9
Counterfeit Prescription Drugs	10
Substandard Prescription Drugs	10
Drug Shortages	12
Environmental Concerns	13
Overmedication and Adverse Drug Reactions	15
KEEPING AN EYE ON APPROVED PRESCRIPTION DRUGS THROUGHOUT THEIR LIFECYCLE – A CONTINUED ROLE FOR THE FEDERAL GOVERNMENT	17
Optimize Electronic Health and Prescription Drug Databases	17
Resolve Cross-jurisdictional Data-Sharing Agreements	19
Address Prescription Drug Abuse, Misuse and Addiction	20
Improve Efforts to Address Antibiotic Resistance	25
Reduce the Exposure of Canadians to Counterfeit and Substandard Drugs	28
Reduce the Impact of Drug Shortages	32
Implement Policies Specific to Environmental Concerns Related to Prescription Drugs	34
Reduce the Risks Associated with Consumption of Multiple Prescription Drugs	35
CONCLUSION	37
APPENDIX A – LIST OF RECOMMENDATIONS	38
APPENDIX B – WITNESSES	43



INTRODUCTION

The Standing Senate Committee on Social Affairs, Science and Technology (“the committee”) has undertaken a four-phase study on prescription pharmaceuticals, as described in the Order of Reference adopted on November 22, 2011. The study was re-established at the beginning of the second session of the 41st Parliament with a new order of reference on November 19, 2013. The committee tabled reports on the first three phases of this study in November 2012, March 2013 and January 2014. These reports were entitled *Canada’s Clinical Trial Infrastructure: A Prescription for Improved Access to New Medicines* (the “Clinical Trials Report”), *Prescription Pharmaceuticals in Canada: Post-Approval Monitoring of Safety and Effectiveness* (the “Post-Approval Monitoring Report”), and *Prescription Pharmaceuticals in Canada: Off-Label Use* (the “Off-Label Use Report”), respectively.¹

Between January 29 and April 30, 2014, the committee heard from witnesses in regard to the fourth phase of this study, the “unintended consequences” in the use of prescription pharmaceuticals. Over the course of 17 meetings, the committee heard testimony from officials from national patient safety and health system organizations; specialists on prescription drug abuse; experts on antibiotic resistance; members of national health professional organizations; representatives of stakeholders in the drug supply chain; officials from First Nations’ groups; researchers and academics with an interest in pharmaceutical policy and the environmental impact of pharmaceuticals; officers from law enforcement agencies; representatives of the drug manufacturing industry; patient advocates; and officials from Environment Canada, Health Canada, the Public Health Agency of Canada and the Canadian Institutes of Health Research.

¹ For more detail, refer to the [Standing Senate Committee on Social Affairs, Science and Technology’s 14th and 20th reports of the 1st session, 41st Parliament](#), which pertain to the first two phases of the prescription pharmaceutical study, and its [5th report](#) of the 2nd session, 41st Parliament, which pertains to the third phase.



CONTEXT

In earlier reports on previous phases of the pharmaceutical study, this committee has discussed Health Canada's role in the approval of prescription drugs for sale in Canada as well as how the department monitors those drugs for safety and effectiveness once they are available to Canadians and consumed for both on- and off-label indications. These earlier reports touched on some of the unintended consequences in the use of prescription drugs, namely adverse

reactions and the consumption of approved medicines for purposes or by sub-groups of the population not indicated in the Health Canada approval for the drug. This report builds upon the foundation set out in these earlier reports, explores additional issues linked to the use of these drugs and makes a number of recommendations to address some of the unintended consequences in the use of prescription drugs that have an impact on the health and safety of Canadians.





UNINTENDED, BUT NOT UNEXPECTED, ISSUES OF CONCERN

ABUSE, MISUSE AND ADDICTION

We now have millions of tablets of what amounts to pharmaceutical grade heroin being dispensed every year in Canada.

— David Juurlink, *Institute for Clinical Evaluative Sciences*

Certain classes of prescription drugs are known to have a high potential for harm as a result of misuse, abuse and addiction. These classes include opioid pain relievers such as oxycodone and morphine; stimulants such as amphetamines; and, sedatives such as benzodiazepines. Collectively these medicines are referred to as psychoactive drugs and although all present a high risk for misuse and abuse, the opioids present a high risk for addiction as well. As such, most witness testimony focussed on this class of prescription pharmaceutical.

Opioids are controlled substances listed in schedule 1 of the *Controlled Drugs and Substances Act* (CDSA). Pursuant to the CDSA, the *Narcotic Control Regulations* stipulate restrictions on and requirements for the production, storage, possession, sale and prescribing of controlled substances, including provisions specific to pharmacists, practitioners and hospitals. As such, prescription opioids, which are largely approved for use in the treatment of moderate to severe pain, are regulated under the CDSA as well as the *Food and Drugs Act* and its regulations.

Despite the heightened regulatory focus on prescription opioids over other classes of prescription pharmaceuticals, the committee heard from several witnesses that use of these drugs has

continued to increase in recent years. Research was presented, based on data from provinces where prescription drug data is collected, that suggested that the rate of prescribing opioids has risen dramatically. For example, David Juurlink, a clinician researcher with the Institute for Clinical Evaluative Sciences, stated that there was an 850% increase in oxycodone prescriptions in Ontario between 1991 and 2007. Oxycodone is the active ingredient in many opioid painkillers including OxyNeo® and Percocet®. The committee heard that this surge in opioid use began in the mid to late 1990s. Until that time, complaints of persistent pain by patients were often addressed by physicians first with anti-inflammatory drugs such as acetaminophen and ibuprofen, which are accompanied with their own potential for adverse reactions, but can be successful in treating mild to moderate pain.

Witnesses indicated that aggressive marketing in the late 1990s by manufacturers of these drugs, including conferences sponsored by the pharmaceutical industry, training and educational materials, was a significant contributor to the increasing number of opioid prescriptions that are written each year. Beth Sproule, a clinician scientist representing the Centre for Addiction and Mental Health, noted that Canada is now the second highest per capita consumer of prescription opioids in the world, behind only the United States. In fact, the International Narcotics Control Board (INCB), which collects data on total narcotic usage in 200 countries and translates this information into per capita usage, has demonstrated that Canadian opioid consumption increased steadily between 2000 and 2011. Canada's ranking went from fifth to second during this time. The committee was told that Canadian doctors now write \$30 billion worth of opioid prescriptions per year.



Several witnesses, including Susan Ulan, Co-Chair of the Coalition on Prescription Drug Misuse, emphasized that prescription opioids have a legitimate therapeutic purpose and that medical access to these drugs is important and in those situations should not be reduced. Canada should not strive to be at the bottom of this INCB ranking as this position suggests poor access to necessary pain medication. However, high consumption rates of pharmaceuticals known to have a significant potential for addiction should be of concern to everyone. Committee members were told that prescription painkillers are estimated to have caused the death of over 10,000 Canadians in the last 20 years, but that such deaths are not specifically tracked. In addition, witnesses noted that opioid deaths represented only a fraction of the lives that have been profoundly affected by these drugs as individuals with opioid addictions struggle in terms of their professional and private lives being turned upside down often before they have been able to get treatment.

The number of lives affected, the number of prescriptions written, filled and consumed, the lives lost, the number of individuals who become addicted to prescription opioids: none of these statistics is available because these data are not systematically collected in Canada. Witnesses spoke of Canada's fragmented system whereby only indirect measures, such as the Canadian Alcohol and Drug Use Monitoring Survey (CADUMS), enrolment in treatment facilities for prescription drug abuse and addiction, levels of criminal activity related to prescription drug use, etc. are the data sources available to stakeholders to alert them to the growing problem of prescription drug misuse, abuse and addiction.

The committee was told that there is no single group responsible for tracking these data, which would involve collaboration among the provinces and territories for data collection. In this regard members heard about the importance of prescription drug monitoring programs, or drug information systems, and the urgent need for all jurisdictions

to implement interoperable schemes. Witnesses noted that implementation of these systems could not only allow for better data collection, but could affect the rate at which opioids are prescribed. This phenomenon was noted when British Columbia's PharmaNet, a centralized database that links all community and hospital pharmacies in that province, was implemented in 1995. The call for interoperable drug information systems has resonated throughout this committee's study on prescription pharmaceuticals.

Several health professionals emphasized that prescribing guidelines for opioids have been issued. The committee heard that the *Canadian Guideline for Safe and Effective Use of Opioids for Non-cancer Pain* was issued in 2010 and will be updated when appropriate. The guideline was accompanied by a knowledge transfer strategy so that physicians could apply the guideline to their practices. Fleur-Ange Lefebvre, Executive Director of the Federation of Medical Regulatory Authorities of Canada explained that this guideline includes the identification of a "watchful dose" of 200mg of morphine per day; a dose that is generally accepted as sufficient to treat most cases of non-cancer pain. The guideline states that prescribers should proceed with caution if they want to increase dosage beyond the watchful dose. Some witnesses questioned whether the watchful dose should be lower; while others pointed out that few prescribers are questioned or challenged if they choose to prescribe opioids in amounts that exceed the suggested watchful dose.

Addiction specialists discussed the increasing rate of addiction to prescription opioids. Although they emphasized that there is no comprehensive surveillance in Canada to define how many individuals are suffering from such an addiction, which regions of Canada are most affected or what the characteristics are of those people who are most at risk, the specialists indicated that it is generally agreed that addiction rates have been increasing in recent years. Cameron Bishop, a representative of Reckitt Benckiser Pharmaceuticals,



pointed out that a 2009 study estimated that between 321,000 and 914,000 non-medical prescription opioid users existed among the general population in Canada. The committee was told that misuse of, abuse of and addiction to prescription drugs affect all communities in Canada and all population groups, and that the problem is not restricted to marginalized sub-groups of the population.

Some witnesses raised concerns over the manner in which Health Canada assesses the safety and effectiveness of drugs. The issue of the generic version of OxyContin® was discussed in this context. That is, despite voluntary withdrawal from the market of OxyContin® by the patent holder Purdue Pharma in response to concerns raised over the high incidence of abuse of and addiction to this drug, Health Canada proceeded soon after these concerns were raised to grant market approval to the generic version of the long-acting opioid.²

The committee heard from some witnesses about the limited availability of non-opioid alternatives because of drug formulary restrictions. Drug formularies provide a list of products that may be reimbursed under a drug insurance program. Peter Doig, President of the Canadian Dental Association, observed with some frustration that the Non-Insured Health Benefits Program (NIHB), which provides financial coverage to First Nations and Inuit for prescription drugs and other medical benefits and services, restricts the non-opioid treatment options available. This restriction, he suggested, results in unnecessarily increasing the number of narcotic prescriptions to this population, leaving individuals more vulnerable to misuse of, abuse of and addiction to these medicines. Although a Health Canada representative testified that neither the brand-name nor generic versions of long-acting oxycodone are listed on the NIHB formulary, the issue of whether the NIHB program encourages,

or even offers, non-opioid alternatives was not addressed.

Finally, the issue of treatment options for prescription opioid addiction was raised by some witnesses. The inherent toxicity of prescription opioids was described as being equivalent to that of “pharmaceutical grade heroin.” In other words, addiction to opiates is no longer limited to illicit heroin; rather it is a pharmacologically equivalent addiction that begins in the doctor’s office with a prescription for a needed medicine. Unfortunately, the stigma is often the same for individuals who have become addicted to prescription drugs as it is for those who have succumbed to street drugs, and patients do not get the sympathy and treatment necessary. Instead, Owen Adams, a Vice President with the Canadian Medical Association, explained that patients will resort to illegal behaviour including doctor shopping, forging prescriptions and acquiring the opioids from street dealers. The committee heard anecdotally of a mother who became addicted to the prescription drugs she was prescribed for back pain. Once addicted, her physician refused to help her because she was told that he does not deal with “people like her”. Consequently, this led her down a very dark road that resulted in her losing her children and her job.

Medication-assisted treatment options for prescription opioid addiction are similar to those used to treat illicit heroin addiction. Specifically, the committee heard about two options that have been approved by Health Canada: methadone and Suboxone®. It heard that methadone, also a CDSA schedule I substance, suppresses opioid withdrawal symptoms, reduces cravings and blocks the effects of the problem opioid. However, methadone must be administered by a practitioner specifically permitted to do so. As methadone is regulated not only under the FDA but also the CDSA, Health Canada approval of methadone includes a stipulation that practitioners must seek a ministerial exemption

² The maker of OxyContin® replaced this drug with a tamper-proof version called OxyNeo®.



pursuant to section 56 of the CDSA. Specifically, section 53(3) of the *Narcotic Control Regulations* prohibits the prescribing, selling, providing or administering of methadone without a ministerial exemption. Like the opioid that produced the initial addiction, methadone has a euphoric effect and can also be habit forming.

A second medication-assisted treatment for opioid addiction, Suboxone[®], was described to the committee. This Health Canada-approved drug contains two components: buprenorphine and naloxone. Buprenorphine is also a Schedule I CDSA drug, but while it produces little euphoric effect it blocks the effects of other opioids. The naloxone component of Suboxone[®] deters abuse of the drug. If Suboxone[®] tablets, which are intended to be absorbed under the tongue, are crushed and snorted or dissolved and taken intravenously, the naloxone precipitates withdrawal symptoms. The Health Canada approval of this product stipulates that prescribers must have experience in medication-assisted treatment for opioid addiction and must complete a recognized Suboxone[®] Education Program.³

While the committee heard that prescription opioid addiction affects all communities in Canada, some witnesses emphasized issues that are particular to First Nations people. With respect to the availability of addiction treatment options, the committee was



told that Suboxone[®] treatment is available under the NIHB by exception only. Carol Hopkins, Executive Director of the National Native Addictions Partnership Foundation, explained that while methadone requires a ministerial exemption, which significantly limits the number of practitioners who can prescribe, sell and administer the substance, Suboxone[®] does not and therefore could be dispensed and administered by a greater number of health providers. Further she described Suboxone[®] as better tolerated and cheaper than methadone.

ANTIBIOTIC RESISTANCE

One of the major unintended consequences of antibiotic use is that we put selective pressure on bacteria, which are only trying to adapt to their environment.

— Philippe Lagacé-Weins, Canadian Antimicrobial Resistance Alliance

Antibiotic resistance is the ability of a bacterial strain to survive exposure to a specific antibiotic. It is not uncommon for a bacterial strain to become resistant to one or more antibiotic treatments but, generally, it will succumb eventually to one of the many antibiotic drugs that are available. Over time several strains of bacteria have developed resistance to multiple drugs, and there is now concern that some strains of bacteria will eventually be resistant to all available antibiotics. In fact, some witnesses suggested that the global problem of widespread antibiotic resistance may well indicate that we are headed for a “post-antibiotic era,” meaning that we may soon not be able to count on antibiotics to cure infections that we have long considered to be treatable.

Some witnesses suggested that antibiotic resistance should not have been unexpected since it involves a well-established process whereby applying

³ Health Canada, Product Monograph for Suboxone[®], 17 June, 2013.



pressure on a bacterial population allows for the selection of organisms that contain a gene, or genes, that allows it to resist the destructive actions of an antibiotic drug. The surviving organisms go on to reproduce while the vulnerable organisms are eliminated by the drug. Unlike humans who reproduce every twenty to forty years, bacterial reproduction is in the order of minutes. On an evolutionary scale, the equivalent genetic changes that can take millions of years in humans can be accomplished in weeks in bacteria.

Witnesses explained that the selective pressure described above is made worse through the over-use, misuse and non-medical use of antibiotics in humans and livestock, which result in accelerating the evolution of antibiotic-resistant strains of bacteria. The committee was told that as much as 50% of antibiotic use in humans and 80% of its use in animals is medically unnecessary. Several witnesses described the over-prescribing of antibiotics because of patient demand and the inability, for a variety of reasons, of physicians to resist those demands. In this regard, witnesses spoke of the need for greater awareness about the role of antibiotics and the dangers of their over-use. With respect to antibiotic use in animals, the committee heard that the non-medical use of antibiotics in food-producing animals is widespread. A large proportion of the antibiotics that are produced is used in agricultural settings and distributed in low doses in animal feed to promote livestock growth.

Witnesses commented that the extent of antibiotic resistance in Canada cannot be reliably determined because of a lack of comprehensive surveillance. The Public Health Agency of Canada has the responsibility for surveillance activities of illnesses that pose a public health threat, including bacterial infections for which antibiotics are the primary treatment. The agency is also tasked with monitoring the emergence of antibiotic-resistant strains of bacteria. Witnesses described PHAC's surveillance programs; namely, the Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS)

and the Canadian Nosocomial Infection Surveillance Program (CNISP).

CIPARS monitors antibiotic use and resistance of a selected number of bacterial strains. The program is designed to allow for several surveillance components to be linked which permits an assessment of the health impacts of antibiotic use in both humans and food-producing animals. Several witnesses commended this program and indicated that CIPARS is well respected on the world stage. Scott McEwan, a Professor in the Department of Population Medicine at the University of Guelph, commented that data from the program provide some indication as to the appearance of resistant bacteria, both in humans and animals, across the country. However, witnesses also pointed out that access to the data from CIPARS is limited and that surveillance data available through PHAC are not up to date. Some witnesses suggested that the data are not being used to their potential as the witnesses were unaware of any actions that have been taken by the agency in response to information obtained by this surveillance program. In fact, PHAC does not post any of its annual, quarterly or summary CIPARS reports on its website. At the time of writing, the most recent annual CIPARS report available by request to the agency was for 2009. Witnesses also noted that CIPARS was intended to have a dual function: monitor the emergence of antibiotic resistant bacteria as well as antibiotic use generally. The committee was told that CIPARS is not effectively monitoring the use of antibiotics, including assessments of what drugs are being used, in what animal populations and for how long. In this regard, some witnesses suggested that Canada's distribution infrastructure doesn't lend itself to collecting this data.

CNISP monitors hospital-acquired bacterial infections and includes a component that measures the rates and trends of antibiotic resistant bacterial infections acquired within the healthcare setting. David Patrick, from the BC Centre for Disease Control, indicated that PHAC has done a good job



with respect to CNISP but urged that the surveillance should provide information about more strains of resistant organisms as well as data on the emergence of such infections within the community, not just healthcare settings. Similar to the complaint about PHAC's CIPARS program, the committee was told that data are not available in a timely and comprehensive manner but is often years late. With respect to surveillance of antibiotic-resistant infections acquired within the healthcare setting in general, the PHAC website lists only one report; *The Canadian Nosocomial Infection Surveillance Program (CNISP) Antimicrobial Resistant Organisms (ARO) Surveillance – 2007 to 2011*. This report, published in November 2013, was available as an archived document by spring 2014. There are also several surveillance results for the Methicillin-resistant *Staphylococcus aureus* strain, but no data more recent than 2009 are available.

In comparison, the committee heard that surveillance of antibiotic resistance and antibiotic use, as well as efforts to reduce antibiotic use, in the European Union are more coordinated than they are in Canada. Sweden and Denmark were the first European countries to take action against the non-medical use of antibiotics in food-producing animals, that is, the use of antibiotics as growth promoters. Sweden was described as the first country to monitor data on antibiotic use in agriculture and the first to initiate, in 1986, a regulated withdrawal of antibiotics as growth promoters.

Denmark was described as having implemented a comprehensive surveillance system and as having taken significant action in the area of antibiotics as growth promoters in food-producing animals. In 1995 Denmark introduced its integrated, cross-sectoral monitoring system called DANMAP, which measures the annual consumption of antibiotics and the prevalence of antibiotic resistant bacteria in animals, food and people in Denmark. As a result of the surveillance, Denmark introduced a ban on the use of antibiotics as growth promoters in food-producing animals in 2000.

In 1999, the European Union created the European Antimicrobial Resistance Surveillance Network, or EARS-Net, which gathers surveillance data from its member countries, each of which has implemented its own surveillance system. Many EU countries have adopted the Danish model. The European Union implemented a ban on antibiotic use as growth promoters in food-producing animals in 2006.

Finally, witnesses voiced their concern that there is little research being conducted to develop new drugs as antibiotic resistance renders more and more approved antibiotics ineffective. In fact, the committee heard that it has been many years since a new antibiotic drug has been approved by Health Canada. Brian O'Rourke, President and CEO of the Canadian Agency for Drugs and Technologies in Health, explained that any newly developed antibiotic would be introduced to the market only as a third-, fourth- or even fifth-line therapeutic option, meaning that it would be used only sparingly. As such, the high cost of drug development coupled with the limited capacity to recoup those costs was the reason cited for the lack of efforts in this area.

COUNTERFEIT AND SUBSTANDARD DRUGS

It is very common that what comes out of China and India just isn't as good as it should be.

— Amir Attaran, University of Ottawa

The committee heard about two issues that have a direct impact on the safety and security of the prescription drug supply in Canada: counterfeit and substandard medicines. Counterfeit drugs refer to products that are presented as approved drugs produced by known manufacturers but that do not contain the specified components and may very well be dangerous to the consumer. These fraudulent products are intentionally produced



and sold to unsuspecting consumers often by unlicensed dealers outside the established drug supply chain.

Substandard prescription drugs are Health Canada-approved medicines that have been produced by a licensed facility but which have been manufactured in breach of the conditions set out in the drug establishment licence or of the processes and specifics listed in the monographs of the authorized products. The production of substandard drugs may be either inadvertent or intentional.

The concerns associated with counterfeit and substandard drugs are addressed separately below.

Counterfeit Prescription Drugs

As described above, a counterfeit drug is a fraudulently produced substance made to look like an approved drug manufactured by an established company. Counterfeit products usually do not contain the appropriate active medicinal ingredients and can sometimes include dangerous components. The committee was told that responsibility for identifying counterfeit products and the companies that make them is shared among Health Canada, the Royal Canadian Mounted Police (RCMP) and the Canada Border Services Agency (CBSA). Health Canada may have reason to alert the enforcement agencies to shipments from a particular vendor, while CBSA can inspect suspect packages at the border and the RCMP conducts investigations of counterfeit products.

The production and sale of counterfeit prescription drugs was described as a global problem that requires collaboration across jurisdictions to combat the problem. In this regard, the committee was told that, since 2008, Canada has participated in an annual week of international action to intercept counterfeit medicines called Operation Pangea coordinated by Interpol. In 2013, this operation resulted in the interception of 238,000 units

of counterfeit as well as illicit medications originating from 19 countries. It was also emphasized that the amount of counterfeit and unlicensed medicines seized during Operation Pangea has increased significantly from one year to the next since 2008 and that between 2008 and 2013 there was a 100% increase in the number of investigations. Routine interception of the postal stream also suggests an increase. The committee was told that during fiscal year 2012-2013, 11,756 counterfeit prescription drugs were intercepted in the postal stream. During the first eight months of fiscal year 2013-2014 about 7,000 counterfeit medicines were intercepted.

While the committee was told that most counterfeit product is imported into Canada in the postal and courier streams, members heard that these products have been purchased via illegitimate online pharmacies, which are often indistinguishable from legitimate online pharmacies. The companies selling counterfeit medicines may present themselves as operating from licensed facilities in highly regulated countries when in fact the committee was told, the main source of counterfeit drugs is Southeast Asia, where witnesses suggested that drug regulation may be lax. In this regard the RCMP indicated that it conducted an investigation into Internet pharmacies between April 2010 and April 2012, called Project Centurion. Under Project Centurion, the RCMP looked into 70 Canadian pharmacy websites and 400 international pharmacy websites, which resulted in 27 investigations. Witnesses noted that although there have been no successful prosecutions to date in Canada of illegal online pharmacies, several Canadians have been successfully prosecuted in the United States for operating such websites and selling counterfeit products.

Substandard Prescription Drugs

The issue of substandard prescription drugs was presented to this committee as an unintended consequence of the globalization of manufacturing



capacity. Drug manufacturing facilities are no longer limited to developed countries. Rather, they are appearing in greater and greater numbers in those countries with developing economies. Unfortunately, many of these countries do not have drug regulatory frameworks that are as stringent as those in developed countries.

In order to streamline inspections and regulatory approvals for drugs that are not manufactured domestically, Health Canada has entered into Mutual Recognition Agreements (MRAs) with several developed countries that it considers to have equivalent Good Manufacturing Practices (GMP) Compliance Programs for pharmaceutical production. An MRA covers the drugs produced in that country as well as those imported into it and which are sent on to Canada. Although there is no MRA with the United States, Health Canada officials have indicated in their statements to this committee that there is agreement between our countries, but the specifics of this agreement were not described.

While drug manufacturers are required to comply with their conditions of licensure, including the conditions of each drug's market authorization and the good manufacturing practices required under their Drug Establishment Licences, Health Canada is responsible for ensuring compliance under its inspections program.

The committee was told that, for drugs manufactured in developed countries, Health Canada relies on MRAs to ensure GMP compliance. Several prescription drugs imported into Canada, however, have been manufactured in countries with which Canada has not entered into MRAs. Health Canada indicated that 50% of foreign sites from which Canada imports medicines are located in MRA countries. Of the remaining 50%, half are in the United States and the remainder of the foreign sites are in non-MRA countries such as India and China.

In terms of the number of drugs imported from foreign sites, Health Canada provided country of origin information to the committee for only 54% of the 15,868 pharmaceuticals currently authorized for sale in Canada, or 8,554 drugs. Of these drugs, 51.6% are domestically produced, 22% are from the United States, 4.6% from India, 4.1% from Germany, 3.3% from the United Kingdom and 3.1% from France. The department further disclosed that between 1% and 3% of medicines come from Puerto Rico, Italy, Switzerland, Ireland and Belgium and that less than 1% comes from each of Australia, Israel, the Netherlands, Denmark and Spain. It is not clear whether these proportions would change if Health Canada had been able to identify the country of origin of all authorized prescription drugs. In fact, Amir Attaran, holder of the Canada Research Chair in Public Health and Global Development Policy at the University of Ottawa, stated that the proportion of imported pharmaceuticals in Canada is not known. He suggested however that it is reasonable to assume that Canada imports at least as much product as the United States, which imports 80% of its medicines and medicinal ingredients, with most of these imported products coming from countries such as China and India.

Regardless of the proportion of Canada's drug being manufactured in non-MRA countries, the committee heard that Health Canada does not focus any inspection programs at facilities in these countries. Unlike the United States Food and Drug Administration that conducts hundreds of inspections at sites outside of the U.S each year, Canada conducted only three foreign inspections in 2011. A Health Canada official indicated that this number had increased to 14 foreign site inspections in 2013-2014.

The committee was told that in several instances drug manufacturing sites in non-MRA countries, particularly India, have been identified by drug regulators in other countries to be non-compliant



with GMP requirements. Of particular concern to the committee was the issue of the generic drug manufacturer Ranbaxy Laboratories Limited, which has a number of facilities in India. Under whistle-blower protection legislation in the United States a former executive with Ranbaxy informed the Food and Drug Administration in 2008 that the drug maker had been deliberately falsifying its records and fabricating data about the medicines it produced. There are still unresolved issues with this company today resulting in bans of its products from certain facilities in the European Union as well as the United States. To date, there has been no action by Health Canada with respect to Ranbaxy which is authorized to market about 160 medicines in this country. According to its testimony to this committee, Health Canada currently lists only one drug manufacturing facility in India, belonging to Apotex Inc., as non-compliant, but it was not clear whether this non-compliance has resulted in a suspension of the drug establishment licence or a temporary ban on importation of its products.

DRUG SHORTAGES

To truly mitigate the consequences of drug shortages, every link, every stakeholder in the supply chain globally and within Canada has a role to play.

— Kathleen Boyle, HealthPRO
Procurement Services, Inc.

Drug shortages have always occurred from time to time, but they have increased in frequency and duration over the last ten or fifteen years. A number of reasons were suggested by witnesses as to what is causing these shortages including active pharmaceutical ingredients being produced in fewer facilities making them vulnerable to operational and regulatory problems; Canada being only a small share of the global market

and subject to market forces; pricing restrictions placed on publicly funded drug programs, discontinuances and unexpected increases in demand.

In response to the growing problem of drug shortages, witnesses told this committee about a number of initiatives that have been pursued to prevent their occurrence and minimize their impact when they do occur. In March 2012 a public website for posting drug shortages was created, which is managed by the pharmaceutical industry. Although drug companies are not required to post drug shortages, they have publicly committed to doing so.

Another step that has been taken was the creation of a Multi-Stakeholder Steering Committee on Drug Shortages (MSSC) in 2012. The MSSC is composed of representatives from pharmacy, pharmaceutical and healthcare associations, the Canadian Agency for Drugs and Technologies in Health as well as Health Canada and provincial representation from Alberta. In 2013 the MSSC issued two documents to improve communication and action plans: *Protocol for the Notification and Communication of Drug Shortages*, and, *A Toolkit for Improved Understanding and Transparency of Drug Shortage Response in Canada*.

In August 2013 the MSSC launched a Contracting and Procurement Best Practices Working Group to examine how prescription drug bulk purchasers and wholesalers could modify their business practices with a view to mitigating drug shortages. In this regard, the committee was told that bulk purchasing contracts for medically necessary drugs is no longer exclusively awarded on the basis of price. Rather, as the committee heard from Kathleen Boyle, a Vice President with HealthPRO Procurement Services, best practice is now considered to be the split-award approach, and not a sole-source contract which leaves the purchaser vulnerable to a shortage should the contracted supplier be unable to deliver the product.



Despite the significant progress that has been made because of the collaborative efforts of many stakeholders, a number of concerns remain. One such concern is that not all stakeholders have been considered in MSSC discussions. The committee was told that practitioners who work in private practice, such as dentists, are not considered in allocation plans when drugs are in short supply. Dental practitioners, who keep only a limited supply of antibiotics, pain relievers, sedatives and anaesthetics on hand, are quickly affected when a drug is not available because supply is focussed on acute-care settings like hospitals during a shortage.

The usefulness of the drug shortages website as it is currently structured was also challenged by several witnesses. In the United States, where suppliers are required to notify the Food and Drug Administration of disruptions, the drug shortages website is managed by the regulator. Further, the committee heard that the Canadian website does not provide much information and is not easily searchable. The U.S. website, for example, provides an alphabetic listing of drug shortages, like the Canadian site, as well as a list categorized by therapeutic class. Unlike the Canadian website the American one also provides the reason for each shortage, such as increased demand, discontinuation or GMP compliance issues.

As such, several witnesses commented that the drug shortages website, drugshortages.ca, could be more useful. The committee learned that anticipated shortages are posted within a couple of days of supply disruption only. In fact, David Johnston, the President and CEO of the Canadian Association for Pharmacy Distribution Management, stated that distributors often only find out about a shortage after a shipment fails to show up. The committee heard that the time frame to manufacture, package and ship pharmaceuticals is in the order of three to four months. Therefore, witnesses suggested, it is not unreasonable for stakeholders along the drug supply chain to request notification

of months and not days, should the disruption occur at the front end of the manufacturing process.

Other witnesses pointed out that there is no guarantee that there will be any notification at all since drug manufacturers are not required to post anticipated shortages. A Health Canada representative indicated that the department has made it clear to the pharmaceutical industry that it expects companies to post all actual and anticipated shortages and pointed to the sharp increase in these postings over the past year as evidence that drug companies are complying.

ENVIRONMENTAL CONCERNS

The acute toxicity is not really the issue. The issue is the low-level exposures over a longer period of time.

— Rebecca Klaper, University of Wisconsin-Milwaukee

The use of prescription pharmaceuticals in Canada has increased steadily over the past few decades, as it has in other developed countries. A significant proportion of these medicines are finding their way into our environment. Consumed drugs are excreted unchanged or in a modified form. Unused drugs are frequently disposed of down the sewer, and then make their way into various bodies of water, or in the garbage which ends up in landfill. With the exception of those drugs that act as endocrine disrupters, there is as yet no evidence that the drugs that are finding their way into our environment are having a negative impact on plant or animal systems. However, that does not mean that such negative impacts may not occur. In this regard, the committee was told that it is necessary to determine the level of these compounds in the environment and assess their impact on plant and animal life.



With respect to monitoring the level of pharmaceuticals in our environment, the committee expected to hear that Environment Canada's Pharmaceuticals and Personal Care Products Surveillance Network is responsible for systematic sampling, testing and public reporting on these environmental contaminants. However, a representative from that department described that program as an informal effort by scientists involved in other surveillance and research programs. In addition, the committee was told that any information that is gathered in this regard is available only in articles that those scientists have published in peer-reviewed journals.

Instead, the committee was told that environmental concerns linked to the disposal of pharmaceuticals are addressed under the Chemicals Management Plan that is a collaborative effort of Environment Canada and Health Canada, as well as under an environmental assessment by Health Canada,

before they are approved for sale in Canada. When asked, the representative from Health Canada did not elaborate on the environmental assessment that the department performs.

Regardless of whether Environment Canada conducts surveillance to gather data on the amount of pharmaceuticals reaching our waterways or research on their environmental impact, the amount of pharmaceuticals that is being released into the environment can be reduced in two ways: implementing sewage treatment systems and reducing improper disposal.

With respect to pharmaceuticals in waste water, the committee learned that these substances are present in parts per trillion, or low parts per billion, which is thousands of orders of magnitude lower than therapeutic dosages. Nevertheless, Wendy Krkosec, a research engineer at the Centre for Water Resources Studies at Dalhousie University,





told the committee that the concern is whether constant exposure to this low concentration can be harmful to plant or animal (including microorganisms) life. Rebecca Klaper, an Associate Professor at the School of Freshwater Sciences at the University of Wisconsin-Milwaukee, stated that although no sewage treatment process could ever completely eliminate this mixture of substances, it is important to monitor the level of these substances, particularly those pharmaceuticals of greatest concern to the environment, and then design sewage treatment processes for those compounds specifically.

Witnesses also noted that new wastewater regulations came into force last year. The *Wastewater Systems Effluent Regulations*, pursuant to the *Fisheries Act*, require sewage treatment plants of a certain size (about one in four Canadian plants) to treat sewage to a specified standard, which is generally considered sufficient to remove biological waste but will not lead to effective removal of pharmaceuticals. The new regulations also include sampling and testing requirements although it is not clear at this point which, if any, pharmaceuticals are to be monitored.

Proper disposal of expired and unused pharmaceuticals is a relatively easy and inexpensive way of reducing the amount of medicines that find their way into the environment. In this regard, the Canadian Generic Pharmaceutical Association and Rx&D both indicated their participation in the Health Products Stewardship Association that funds “Take Back” programs in various locations across Canada. Take Back programs encourage consumers to bring their unused and expired medicines in to specified locations for proper disposal. This can be done either by requesting that drugs be brought to a central location or by encouraging pharmacists to accept returns and send them on to a central location for disposal. Despite these efforts as well as the establishment of a National Prescription Drug Drop Off Day,

witnesses observed that only a small proportion of unused and expired medicines is disposed of under these programs.

OVERMEDICATION AND ADVERSE DRUG REACTIONS

We have created a love affair with drugs.

— Hugh MacLeod, Canadian Patient Safety Institute

The reports for the three previous phases of the committee’s pharmaceutical study each discussed the potential for adverse drug reactions (ADRs). ADRs may become apparent during the clinical trials of candidate drugs or they may be noted only once new drugs are released for use in the general population and used for longer periods of time. This committee’s report on off-label pharmaceutical use highlighted the additional issue of adverse reactions that may arise when drugs are used for off-label purposes or in sub-groups of the population not approved in a product’s market authorization.

The potential for ADRs increases with the number of medicines consumed. For the elderly, the number of drugs consumed can be relatively high. John Wright, President and CEO of the Canadian Institute for Health Information, revealed that seniors are the most likely sub-group to be overmedicated. He indicated that 70% of Canadian seniors are taking five or more medicines, while nearly 10% of seniors are being prescribed 15 or more drugs. He further stated that 10% of seniors living outside long-term care facilities consume at least one drug that is considered to be potentially dangerous. As a result, seniors are five times more likely than other Canadians to be hospitalized as a result of an adverse drug reaction.



Access to patient data is necessary in order to determine whether an adverse reaction is attributable to a specific drug; a drug-drug interaction; a drug-food interaction; or a complication from a co-morbid condition. Unfortunately, researchers find that access to such data is difficult. Michal Abrahamowicz, a professor in the Department of Epidemiology at McGill University, expressed frustration that queries from the federal government on a drug's safety and effectiveness can require complex negotiations with provincial governments in order to get access to necessary data. He indicated that some jurisdictions are very reluctant to allow access to data that are completely anonymized and therefore not a threat to privacy breaches.

In response to the accepted observation that an increase in the number of prescribed medicines carries a greater potential for adverse reactions, the committee heard from several witnesses that there needs to be more focus on this issue in: the curricula offered at medical schools in Canada; continuing education programs; collaboration with other healthcare providers, particularly prescribers; standardization of optimal prescribing practices across jurisdictions; and routine medication reviews. In terms of medication reviews, the committee was told by Phil Emberley, a Director with the Canadian Pharmacists Association, that this is an area in which pharmacists could provide some expertise.





KEEPING AN EYE ON APPROVED PRESCRIPTION DRUGS THROUGHOUT THEIR LIFECYCLE – A CONTINUED ROLE FOR THE FEDERAL GOVERNMENT

Despite the range of issues addressed during the final phase of the committee’s pharmaceutical study, two concepts emerged that were relevant to more than one issue: the need to enhance awareness and the need for improved surveillance and data collection.

In terms of awareness, some witnesses noted that public campaigns to highlight the unintended consequences of consuming opioid pain relievers; excessive use of antibiotics; counterfeit medicines; and improper drug disposal would encourage consumers to take actions that promote safe prescription drug use both for themselves and the environment. Awareness campaigns for health professionals, either as a component of their training or within the continuing education format, were also identified as necessary components of a comprehensive response to the issues listed in this report.

In terms of data collection and surveillance, the committee heard that these are not satisfactory in a number of areas. For example, as noted earlier in the report, with respect to prescription drug abuse and addiction, witnesses indicated that complete data are not available for the number of people affected, the most frequent prescribers, the number of addiction-related deaths, the rate of prescribing opioids, etc. Similarly, the committee was told that although the Public Health Agency of Canada is responsible for collecting data on

antibiotic use and resistance, these data are not available in a timely fashion and are not easily accessible.

Awareness campaigns and data collection will be explored further under the relevant categories below.

OPTIMIZE ELECTRONIC HEALTH AND PRESCRIPTION DRUG DATABASES

Health care professionals need electronic health records with clinical decision support systems that allow electronic prescribing to improve quality of care, avoid preventable drug-related morbidity and provide value for money from pharmaceutical expenditures.

— Ingrid Sketris, Health Council of Canada

Canada lags behind other developed countries with respect to electronic formats for health records and drug databases. Ingrid Sketris, a councillor with the Health Council of Canada, revealed that Canada ranks seventh among ten industrialized countries with respect to electronic prescribing.⁴ She also indicated that the rate of electronic prescribing across Canada varies; for example, it has been adopted by only 10% of prescribers in Newfoundland while 58% of

⁴ The nine other countries were Australia, Germany, the Netherlands, New Zealand, United Kingdom, France, Switzerland, Norway and the United States.



prescribers in Alberta have accepted it. As a result of the poor access to patient data, the committee was informed that Canada ranks ninth out of ten countries on how easily a list of a patient's medications can be generated.

This committee has made repeated calls for the implementation of electronic health databases. In its 2012 report entitled *Time for Transformative Change; A Review of the 2004 Health Accord* this committee urged increased investment, implementation and uptake of such databases. This committee has also recommended in reports on earlier phases of this study that Canada must accelerate its implementation of electronic databases. It has recommended that Health Canada encourage all provinces and territories to implement electronic

prescribing, that all prescription drug dispensaries be linked to a central system within each jurisdiction and that electronic health records be linkable to and compatible with the electronic prescription drug data system. During the current phase of the study, the importance of drug information systems, or prescription drug monitoring programs, was made even more apparent to committee members. Assessments of drug-drug interactions, prescription drug consumption trends, alerts about drug shortages and suggestions of therapeutic alternatives can all be facilitated by optimized electronic health and prescription drug databases.

While witnesses suggested that work is continuing in jurisdictions across Canada to achieve full coverage of electronic medical records, electronic





The committee therefore recommends that the Minister of Health — in conjunction with recommendations 9, 10 and 11 of the committee’s *Post-Approval Monitoring Report* regarding electronic medical records, electronic health records and provincial drug information systems, and with recommendation 1 of the committee’s *Off-label Report* regarding electronic prescribing — take an active role in working with the provincial and territorial governments to:

- **Establish targets for the implementation of each electronic health and prescription drug system;**
- **Promote the use and accelerate uptake of these databases by health professionals through an aggressive targeted awareness campaign; and,**
- **Report publicly on the progress of implementing electronic health and prescription drug systems. [Recommendation 1]**

health records and drug information systems, the committee agrees that progress has been too slow. In this regard, the committee believes that Health Canada must take a more active role in overseeing the implementation of these databases and in ensuring that all Canadians are covered.

RESOLVE CROSS-JURISDICTIONAL DATA-SHARING AGREEMENTS

Better data, better decisions and healthier Canadians.

— John Wright, Canadian Institute for Health Information

The committee shares in the frustration expressed by several witnesses that health data are not easily shared among jurisdictions and that access to data can sometimes be stalled because of privacy and confidentiality issues. It is clear from committee testimony that individual research institutes, such as the Institute for Clinical Evaluative Sciences in Ontario, are able to access anonymized provincial data while researchers wanting access to Canada-wide data are met with resistance. Even national agencies like the Canadian Institute for Health Information are limited in their capacity to access data across jurisdictions. Patient advocates, namely Sholom Glouberman, President of Patients Canada and Colleen Fuller, the Chair of PharmaWatch Canada, agreed that the collection of data is essential but is hampered because of a lack of sharing among provincial databases and central agencies. The committee is optimistic that implementation of electronic health records and drug information systems across Canada coupled with the proper anonymization of personal information will remove the barriers to data sharing across jurisdictions.



The committee therefore recommends that the Minister of Health urge provincial and territorial Ministers of Health to ensure access to anonymized health data by those agencies, institutes and researchers whose responsibilities require such access.

[Recommendation 2]

ADDRESS PRESCRIPTION DRUG ABUSE, MISUSE AND ADDICTION

Substance abuse is a problem too complex, too significant and too deeply rooted to be solved by one group or approach.

— Robert Eves, Canadian Centre on Substance Abuse

Committee members, like so many other Canadians, are very concerned about the increasing consumption of prescription opioids. It commends the diligent work of stakeholders for the March 2013 report entitled *First Do No Harm: Responding to Canada's Prescription Drug Crisis*. This report was issued by the National Advisory Council on Prescription Drug Misuse, with co-chairs from the Canadian Centre on Substance Abuse and the Coalition on Prescription Drug Misuse and made 58 recommendations including proposals for a ten-year pan-Canadian strategy to

combat the problem.⁵ This comprehensive work followed years of studies signalling the crisis as well as some provincial government reports on the issue.

The committee is pleased that Health Canada has initiated action to address this crisis. In January 2014, the Minister of Health, the Honourable Rona Ambrose, co-hosted a symposium on prescription drug abuse with the Canadian Centre on Substance Abuse.⁶ In February 2014, the federal government tabled Budget 2014, which provides for an investment of \$44.9 million over five years to expand the National Anti-Drug Strategy so as to incorporate prescription drug abuse.⁷

As the federal government moves forward on this issue, committee members agree that public awareness campaigns must be included for a comprehensive response to this alarming situation. As well, the committee again wants to emphasize the importance of data collection and surveillance. It notes that no problem can be resolved if it cannot be properly defined. As such, it reiterates its call for standardized drug information systems in all provinces and territories, with access to relevant data granted to specific users. Once implemented, prescription opioid use can be monitored across jurisdictions and areas of high usage as well as products of highest use can be identified.

The committee heard compelling testimony that some physicians are over prescribing opioids for pain and that they may not be well-trained in recognizing the benefit of non-opioid products for general pain maintenance. Further, the committee heard that some patients may pressure physicians

⁵ National Advisory Council on Prescription Drug Misuse, *First Do No Harm: Responding to Canada's Prescription Drug Crisis*, March 2013.

⁶ Health Canada, *Minister Ambrose Co-hosts Symposium on Prescription Drug Abuse*, 24 January 2014.

⁷ *Federal budget 2014: The Road to Balance – Creating Jobs and Opportunities*, pp. 196–197.



to prescribe opioids when they are not essential and that some physicians may yield to patient requests. These issues relate to both training and the practice of medicine which fall within the authority of the faculties of medicine, the medical societies, regulatory bodies and medical training programs. The committee urges in the strongest possible terms that the Canadian Medical Association as well as other stakeholder groups associated with prescriber and dispenser practice to act quickly to address the overuse of opioids.⁸ Special attention must be paid to alternate approaches for First Nations that are culturally sensitive.

The committee therefore recommends that Health Canada post regular updates on its website regarding its progress towards expanding the National Anti-Drug Strategy to include prescription drug abuse.

[Recommendation 3]

The committee further recommends that the prevention component of the expanded National Anti-Drug Strategy require that;

- **Health Canada develop and implement Canada-wide public awareness campaigns on the risks and harms of prescription drug abuse; and,**
- **The Minister of Health work with provincial and territorial Ministers of Health and stakeholders including the College of Family Physicians of Canada, the Royal College of Physicians and Surgeons of Canada, the Federation of Medical Regulatory Authorities of Canada and the Association of Faculties of Medicine of Canada, to optimize physician education and training regarding prescription drug abuse and addiction; and,**
- **The Minister of Health work with interested stakeholder groups to identify opportunities for pharmacist involvement.**

[Recommendation 4]

⁸ The committee notes that, following the drafting of this report, the Minister of Health issued a [Call for Proposals](#) to improve prescribing practices in this area.



The committee further recommends that ongoing discussions related to the expansion of the National Anti-Drug Strategy include negotiations with all jurisdictions to ensure access to data on prescription opioid use for those stakeholders involved in assessing the problem of prescription drug abuse. [Recommendation 5]

The committee therefore recommends that Health Canada include a prescription drug's potential for addiction as part of the department's assessment of a drug's safety and effectiveness such that addictiveness is noted as one of the risks associated with using the drug. [Recommendation 7]

The committee further recommends that Health Canada, through its representation on the Board of Directors at the Canadian Institute for Health Information (CIHI), urge that CIHI be mandated to track, and regularly report on, prescription drug use, particularly use of those drugs that have been identified as having a high potential for misuse, abuse and addiction based on information from provincial/territorial drug information systems.

The committee further recommends that Health Canada reassess the safety and efficacy profile of any approved drug that has a high potential for addiction.

[Recommendation 8]

[Recommendation 6]

Committee members are of the view that more can be done by the drug regulator to heighten the awareness of consumers, prescribers and dispensers to the potential harms of prescription opioids, which are well known to be addictive. As such, members agree that addictive potential should be treated as a possible adverse reaction and incorporated by Health Canada into the safety and efficacy profile of each opioid that the department assesses for market approval.

As noted earlier, prescription opioids are controlled substances and are essentially prescription-grade heroin. As several witnesses pointed out, products regulated under both the *Food and Drugs Act* and the *Controlled Drugs and Substances Act* should be subject to highly stringent restrictions. Based on the increasing rates of addiction to these substances, a rising death toll from such addictions and the rising rate of prescribing these drugs while the rate of prescribing non-opioid alternatives goes down, the committee believes that it is reasonable to conclude that the restrictions currently in place to control the use of prescription opioids are not sufficient. A Health Canada representative stated that the department's decision to grant market authorization to generic long-acting oxycodone, despite the voluntary removal of OxyContin® from the market by the patent holder, was accompanied by new restrictions. These restrictions included only a requirement to submit reports to Health Canada of loss and theft of the product or



of suspicious or unusual activities related to the product. The committee commends these additional measures but suggests that these restrictions are not sufficient. In fact, they do little to protect the health and safety of Canadians, but rather serve only to monitor the rise in addiction to prescription drugs.

In order to better protect Canadians, some witnesses testified that tamper-resistant technologies could be used for most, if not all, prescription opioids. The witnesses suggested that tamper-resistance could be a condition for market approval of such drugs. Implementation of this policy would help to reduce the improper use of the drugs, although it would not affect the drug's addictive nature. As such, members of the committee are of the view that prescription drugs that have the potential for abuse, and that are addictive, controlled substances must be clearly identified. The committee notes that under the *Narcotic Control Regulations* pursuant to the *Controlled Drugs and Substances Act*, the Minister of Health has the authority to place restrictions on practitioners and pharmacists in terms of prescribing and selling these drugs.

The committee therefore recommends that, as a condition of market approval, all prescription opioids that have a potential for abuse be required to incorporate tamper-resistant technology in their design. [Recommendation 9]

A specific discussion is necessary about prescription drug abuse and addiction among First Nations. Committee members were alarmed to hear that Health Canada does not fund any ongoing programs to combat the rising rates of prescription drug addiction among First Nations people, despite repeated calls from First Nations for departmental

The committee further recommends that Health Canada extend the requirement for “Black Box” labelling noted in recommendation 17 of the committee’s *Post-Approval Monitoring Report* to those drugs of high addictive potential.

[Recommendation 10]

The committee further recommends Health Canada implement requirements under the *Narcotic Control Regulations*:

- **specifying the comprehensive information, including cautions regarding addiction and abuse potential, that must be provided to consumers by practitioners and pharmacists; and,**
- **restricting opioid prescriptions to the 200mg “watchful dose” identified in the *Canadian Guideline for Safe and Effective Use of Opioids for Non-cancer Pain*.**

[Recommendation 11]

attention to this matter. Stan Beardy, Ontario’s Regional Chief for the Assembly of First Nations, stated that sustainable funding is required for community-based addiction services. The committee expects that the expanded National Anti-Drug Strategy is to include additional addiction services for the First Nations population; however it is not clear whether the additional \$44.9 million over five years for the expansion will include sufficient funds dedicated to First Nations addiction services.



Witnesses raised a serious concern regarding the pain-reliever options available to prescribers who treat First Nation clients. As described earlier in the report, Health Canada's Non-Insured Health Benefits (NIHB) Program provides financial coverage for prescription drugs. However, coverage is usually limited to those products listed on the NIHB formulary, although coverage is sometimes extended to other drugs on a case-by-case basis. Although a Health Canada representative assured the committee that the NIHB does not list on its formulary the generic long-acting oxycodone, no information was provided related to the criticism that the NIHB formulary does not provide sufficient access to non-opioid alternatives. In addition, the committee questions the status of the Suboxone[®], which was described by some witnesses as a less problematic opioid as it does not produce strong euphoria therefore discouraging abuse. The committee notes that the Minister of Health stated in May 2014 that the Assembly of First Nations and Health Canada intend on launching a joint review of the NIHB program sometime after summer 2014.⁹



The committee therefore recommends that the expansion of the National Anti-Drug Strategy;

- **Provide adequate and sustained funding for prescription drug addiction services for First Nations; and,**
- **Provide physicians serving First Nations' communities with culturally-sensitive pain management training, including the use of non-opioid options.**

[Recommendation 12]

The committee further recommends that Health Canada's review of the Non-Insured Health Benefits program:

- **include in its review of the drug formulary, a thorough assessment of all pain relievers, both prescription and non-prescription, with a view to encouraging the use of non-opioid alternatives wherever appropriate;**
- **include a requirement that tamper-resistant opioids be listed in preference to products without tamper-resistance;**
- **include an analysis of the current "limited use" status of Suboxone[®]; and,**
- **be completed and reported publicly on an urgent basis.**

[Recommendation 13]

⁹ House of Commons Standing Committee on Health, *Evidence*, 2nd Session, 41st Parliament, 15 May 2014.



IMPROVE EFFORTS TO ADDRESS ANTIBIOTIC RESISTANCE

There is a heightened awareness among care providers and the public, but there's room for more education.

— Michael Gaucher, Canadian Institute for Health Information

The committee questions the Public Health Agency of Canada's (PHAC) commitment to addressing antibiotic resistance given the assertion by witnesses that Canada performs poorly in its efforts to conduct surveillance in this area. Specifically the committee notes that the Canadian Committee on Antibiotic Resistance, which was created in 1998, was disbanded in 2007. This decision was taken with the understanding that a more comprehensive approach was needed to address the complex issue of antibiotic resistance; however, witnesses noted, that no action has been taken since to implement a more comprehensive approach. In fact, the national strategy that had been proposed by the Canadian Committee on Antibiotic Resistance has never been implemented.¹⁰

With respect to a comprehensive approach, the committee is impressed with efforts, outlined earlier in this report, by the European Union, initiated by Sweden and Denmark, to slow down the emergence of antibiotic resistance. In contrast, it is disappointed in the passive approach taken by the PHAC. In this regard it notes the frustration of John Conly, an infectious disease physician with Alberta Health Services, who said that there has been a relative lack of activity by PHAC to coordinate the necessary activities to combat antibiotic resistance. While a representative of PHAC suggested that the agency is held up as a model in the global community in terms of antibiotic surveillance, the committee also heard

that this may have been the case a one time, but that it is no longer true. The committee is discouraged that while other countries are focussing resources on comprehensive surveillance, PHAC's role in carrying out this activity appears to have declined. The committee agrees with witnesses who suggested that PHAC should be mandated to coordinate with the provinces to collect surveillance data in order to provide a comprehensive assessment of antibiotic use and the emergence of antibiotic resistance. The committee notes the World Health Organization report issued in May 2014 entitled *Antimicrobial Resistance – Global Report on Surveillance*.¹¹ This report calls for comprehensive surveillance of antibiotic resistance in humans as well as in food-producing animals.

The agricultural sector accounts for a large proportion of all antibiotics used in Canada, most of which are used for non-medical reasons and primarily as growth promoters in food-producing animals. Millicent Toombs, a Director with the Canadian Medical Association, pointed out that the organization has repeatedly called for a reduction in the non-medical use of antibiotics in the agricultural sector. As well, some witnesses suggested that there is a "personal use" loophole in the *Food and Drug Regulations* that permits the unrestricted importation of antibiotics. However, a Health Canada representative asserted that this situation applies only to over-the-counter drugs and not prescription drugs, but that the department is working with provincial counterparts to assess the amounts being brought across the U.S. border. With respect to reducing antibiotic use in food-producing animals, the committee notes that the United States Food and Drug Administration announced in 2012 that it was implementing a voluntary initiative to phase out the use of medically important antibiotics as growth promoters in food-producing animals.¹² The committee notes

¹⁰ Canadian Committee on Antibiotic Resistance, *National Action Plan to Address Antibiotic Resistance*, August 2004.

¹¹ World Health Organization, *Antimicrobial Resistance – Global Report on Surveillance*, May 2014, pp.232.

¹² U.S. Food and Drug Administration, *FDA takes steps to protect public health*, 11 April 2012.



that Health Canada made an announcement in April 2014 about a new policy aimed at reducing the use of antibiotics as growth promoters,¹³ and acknowledges the recent media reports that the Chicken Farmers of Canada is instituting a mandatory ban on injections into eggs of the medically important antibiotic ceftiofor.¹⁴ However, there are numerous players and jurisdictional issues involved when considering the use of antibiotics for agricultural purposes. Given the lack of information the committee was provided in this complex area, it is difficult to effectively assess the actions that need to be taken, or the authorities responsible for taking those actions. As well, members are uncertain that these initiatives, as currently described, will lead to the necessary reduction in antibiotic use in food-producing animals.

Of equal concern as the loss of effectiveness of existing antibiotics is the dearth of research on the development of new antibiotics. Regardless of the efforts to slow down antibiotic resistance, the resistance cannot be stopped altogether. As such, there will continue to be a need for new antibiotics and members agree with the witnesses it heard from on this issue that research and development must be encouraged. In this respect, the committee

notes that the Canadian Institutes of Health Research has invested in antimicrobial resistance. Specifically, the representative from funding agency indicated that \$15 million in 2012-13 was invested in this area.

The committee notes, however, that the United States Food and Drug Administration has implemented incentives in this respect. In 2012, *the Generating Antibiotics Now Act*, which amends the *Federal Food, Drugs and Cosmetics Act*, was enacted. It provides for special designation of “Qualified Infectious Disease Products”, which, upon designation, are entitled to an expedited review by the Food and Drug Administration for market authorization. In addition, the special designation provides for an additional five years of market exclusivity, however it also requires that a reassessment of the product’s safety and effectiveness be conducted five years after receiving market authorization. Finally, the *Generating Antibiotic Incentives Now Act* includes provisions requiring the Food and Drug Administration to provide guidance on the design of the subsequent clinical trials.¹⁵ Under this new regime, a new antibiotic has been developed and has recently been approved in the United States.¹⁶



¹³ Health Canada, *Notice to stakeholders: Collaborative efforts to promote the judicious use of medically-important antimicrobial drugs in food animal production*, 10 April 2014.

¹⁴ Chicken Farmers of Canada, Questions and Answers, “[What are Category I antibiotics and why are they important?](#)”

¹⁵ United States Federal Code of Statutes, Title 21, Chapter 9, *Federal Food, Drug and Cosmetic Act*, §355f, §360a and §360n-1.

¹⁶ United States Food and Drug Administration, *FDA approves Dalvance to treat skin infections*, News Release, 23 May 2014.



The committee therefore recommends that the Public Health Agency of Canada establish a multi-disciplinary, inter-agency group tasked with implementing a national action plan to address antibiotic resistance, as outlined by the Canadian Committee on Antibiotic Resistance in 2004. The action plan must include:

- a national public awareness campaign on the causes and consequences antibiotic resistance;
- renewed surveillance efforts, including a requirement that the Public Health Agency of Canada work with the provinces and territories to require that hospitals collect data and report on antibiotic use and the emergence of antibiotic-resistant bacteria; and,
- a mandate for the Public Health Agency of Canada to assemble, analyse and report publicly on these data, much like the model of the European Union.

[Recommendation 14]

The committee further recommends that the federal government:

- develop and implement a policy, in collaboration with and acknowledgment of the numerous parties involved, to ban or substantially reduce the use of antibiotics as growth promoters in food-producing animals; and,
- post regular updates on all relevant federal government websites on the progress of implementing its new policy which aims to reduce the use of antibiotics as growth promoters in food-producing animals. [Recommendation 15]



The committee further recommends that the federal government encourage research into the development of new antibiotics in a variety of ways, including but not limited to:

- **exploring incentives for the pharmaceutical industry such as extended market exclusivity, priority review and guidance on clinical trial design, to acknowledge the limited market for new antibiotics that would likely not be a first line therapy; and,**
- **creating a funding program specifically for antibiotic development at the Canadian Institutes of Health Research.**

[Recommendation 16]

REDUCE THE EXPOSURE OF CANADIANS TO COUNTERFEIT AND SUBSTANDARD DRUGS

A large number of pharmacies purport to be operating in Canada... [but]... they are actually located in a foreign country offshore somewhere.

— Martin Bolduc, Canadian Border Services Agency

Committee members are discouraged that, despite the successful efforts of the Royal Canadian Mounted Police and the Canada Border Services Agency to identify, seize and investigate alleged counterfeit prescription medicines, the committee

did not receive specific data on the number of prosecutions. Officials from Health Canada stated that the penalties provided for under the *Food and Drugs Act* are not substantial and the committee was told that no prosecutions have occurred under that Act. The committee notes that the *Food and Drugs Act* provides for a maximum penalty of no more than three years imprisonment or a fine not exceeding \$5,000, or both. The committee is encouraged by the federal government's recent efforts to update Canada's drug legislation with the introduction of Bill C-17, an Act to amend the Food and Drugs Act. This bill proposes to increase the penalties provided for under the *Food and Drugs Act* however, it does not include a provision specifically prohibiting the manufacture, storage, packaging, labelling, and sale of counterfeit drugs, which would introduce an additional offence for prosecution.

However, counterfeiting is also captured under the *Criminal Code* and the *Copyright Act*, which carry more substantial penalties and witnesses indicated that prosecutions may have been successful if charges were laid under one or both of these statutes instead of the *Food and Drugs Act*. However, the committee was not told whether prosecutions under the *Criminal Code* or the *Copyright Act* related to the counterfeiting of prescription drugs act as a sufficient deterrent.

The sale of counterfeit prescription drugs is conducted largely via illegitimate internet pharmacies. The committee is concerned that there appears to be little ongoing effort made to identify these websites and that there have been no prosecutions of these fraudulent businesses within Canada despite successful prosecutions of Canadians in the United States. The committee understands that it is difficult to control and legislate against activities beyond our borders and it suggests that any progress on this file will require international collaboration.



The committee therefore recommends that the Minister of Health consult with stakeholders and review the issue of Internet pharmacies operating in Canada that are selling unapproved medicines with a view to implementing the necessary changes, whether they be legislative, regulatory or other, so as to facilitate the successful prosecutions of these enterprises.

[Recommendation 17]

The committee further recommends that the Minister of Health, along with law enforcement and border security organizations, engage international counterparts in discussions to develop and enter into an international treaty to facilitate prosecutions for the counterfeiting of prescription drugs globally.

[Recommendation 18]





The committee further recommends that Health Canada implement a public awareness campaign warning of the risks of purchasing prescription drugs from online pharmacies.

[Recommendation 19]

The issue of substandard prescription medicines is a particular concern for this committee. Most of the drugs consumed in Canada are generic versions, and a substantial number of generic drugs are produced in countries, in whole or in part, with which Canada has not entered into a Mutual Recognition Agreement. With the exception of the United States, these countries are often those with developing economies and drug regulatory frameworks that do not meet the same high standards as those of Canada, the United States, Australia and the European Union. Of such countries, India and China manufacture and export to Canada a significant quantity of drugs. The committee feels that it is essential that Health Canada place additional focus on regulating these imports. Members are uneasy that Health Canada offers apparently contradictory statements in this regard. The committee heard that Health Canada relies heavily on the information gathered by its MRA partners regarding drug manufacturing facilities in non-MRA countries. However, despite Canada's MRA partners banning the sale of products made by Indian-based drug manufacturer Ranbaxy because the company had confessed to

fabricating data, Health Canada took no action on this issue. A Health Canada representative assured members that the department has many communication options in order to address any safety issues that may arise, including Foreign Product Alerts. However, the department has issued no communications regarding ongoing problems with Ranbaxy despite considerable information available to the public via the media and other drug regulators all while numerous products from the company remain for sale in Canada. As such, the committee questions Health Canada's commitment to transparency and openness.

The committee is intrigued by the European Union's policy on batch testing and certifying medicines for sale that have been imported from non-MRA countries. In this regard, it heard that several countries employ Raman spectroscopy (a technology that measures the change in light that is passed through a substance since its interaction is unique to each substance) as a relatively easy and quick means of analysing substances, not only for substandard but counterfeit product as well. A representative of Health Canada indicated that there is a pilot program currently in Canada to assess this approach. Members are supportive of a batch-testing approach for medicines imported from non-MRA countries (excluding the United States). The committee notes Health Canada's poor record of inspecting foreign sites and its inconsistency in adopting measures taken by its MRA partners. Further, members question why the department could only provide country-of-origin information to this committee for just over half of the almost 16,000 drugs currently authorized for sale in this country.



The committee therefore recommends that the Minister of Health direct Health Canada to immediately develop and implement a new inspection policy for drug manufacturing sites which:

- mandates increased inspection activity by Health Canada, either alone or in collaboration with MRA partners, as well as the United States, of sites in countries whose regulatory system is not recognized by Health Canada as equivalent;
- prohibits the use of records as the only information used for inspections but rather requires that inspections involve on-site, physical examinations;
- requires public reporting on the results within one year of these site inspections; and,
- commits to reporting publicly any non-compliance issues detected by the inspection activities of drug regulators of other jurisdictions for sites for which a Canadian Drug Establishment Licence has been issued. [Recommendation 20]

With respect to both counterfeit and substandard medicines and the need to assess the scope of the problem in Canada, the committee urges focussed surveillance and data collection.

The committee therefore recommends that the Minister of Health:

- establish an inter-agency task force which includes relevant representation from federal and provincial health and law enforcement agencies and the Canada Border Services Agency, to assess imported drugs, determine which types of drugs are most often counterfeited or not meeting GMP standards and determine the countries in which those drugs are being manufactured;
- provide the task force with the authority to create advisory bodies composed of experts from the pharmaceutical industry, academia, etc.;
- report publicly on the findings of the task force; and,
- determine the regulatory, inspection and enforcement actions necessary to address the issue of counterfeit and substandard medicines.

[Recommendation 21]



The committee further recommends that Health Canada:

- **report publicly on its pilot program that randomly samples and tests medicines at the border using Raman Spectroscopy, including Health Canada's intentions as to whether to implement the use of the technology on a permanent basis; and,**
- **Ensure, in collaboration with its European Union and United States partners, that all batches of imported prescription pharmaceuticals are tested.** [Recommendation 22]

REDUCE THE IMPACT OF DRUG SHORTAGES

In a survey of physicians conducted by the CMA in September 2012, two thirds of respondents said the shortage of drugs was a significant issue in terms of its impact on patient care and outcomes.

— Owen Adams, Canadian Medical Association

Drug shortages will continue to be a reality. As such, it is imperative that strategies be put in place to minimize their impacts. In this regard, the Multi-Stakeholder Steering Committee on Drug Shortages (MSSC) established in 2013 has taken positive steps towards providing the tools for all stakeholders to minimize the impact of shortages. While noting the concern expressed by some

witnesses that non-primary care providers should be included in policy discussions pertaining to drug shortages, the committee applauds the work of the MSSC and its working groups and encourages all players in the drug supply chain to embrace the strategies and tools that it has identified for mitigating the impacts of drug shortages.

However, some concerns about drug shortages remain for committee members. Diane McArthur, Assistant Deputy Minister with Public Drug Programs Division of Ontario's Ministry of Health and Long-Term Care, pointed out that manufacturers do not give advance notification when a drug is to be discontinued. She noted that these decisions are made well in advance of a drug disappearing from the market and public notification should be given in order to allow practitioners to transition their patients onto alternative therapies. The committee understands that manufacturers are currently required under the *Food and Drug Regulations* to notify Health Canada about drug discontinuances.¹⁷ However, this notification is required only within 30 days of a drug being discontinued.

As well, committee members remain concerned about the industry-run drug shortages website. Complaints by witnesses about the timeliness of drug shortage information, as well as frustration that the database does not provide much information and is not user-friendly need to be addressed urgently. The committee is also uncertain what actions Health Canada can take to oblige the industry to improve the website under the current regulatory framework. Finally, the committee acknowledges Health Canada's recent announcement that a Public Notification Register for Drug Shortages is to be launched soon on the Health Canada website. This Register is described as a site for posting the letters from drug manufacturers committing posting drug shortages on the drug shortages website. Health Canada announced in 2012 that it had secured this

¹⁷ *Food and Drug Regulations*, C.01.014.7



commitment from them. The Register would also include letters sent by Health Canada to manufacturers that have failed to provide timely, comprehensive, and reliable notification through the drug shortages website. Despite the departmental representative's assertion that Health Canada would "take further steps" should drug makers be found not to be accountable and transparent about shortages, the committee is sceptical that any substantive action can be taken under the current regulatory framework and given the numerous criticisms of the drug shortages website but notes that Health Canada has launched a public consultation on the current approach to drug shortages.¹⁸

Finally, the committee has concerns about the identification of therapeutic alternatives during drug shortages. Testimony was not consistent when witnesses were asked which organization should be responsible for this critical function. Health Canada suggested that drug manufacturers should identify alternative suppliers of generic drugs, representatives of the drug industry stated that it is the responsibility of prescribers in consultation with their patient to identify other therapies, while Janet Cooper, a Senior Director with the Canadian Pharmacists Association, countered that while health professionals may have the expertise, carrying out that function would be a waste of healthcare resources. The committee notes that the MSSC's 2013 Toolkit document indicates that the MSSC has appointed a working group that has committed to providing clinical information on therapeutic alternatives through the drug shortages website.¹⁹ The identification of alternative drugs is also essential for reimbursement purposes for public drug programs. The committee is troubled that alternative drugs may not be on the formularies

of public drug programs, including the formularies of federal groups such as the NIHB program for First Nations and Inuit. While witnesses stated that these programs can take measures to add alternative drugs to list, either permanently or for the duration of a shortage, committee members heard that this administrative decision can take several days. Given the frequency of drug shortages, the committee suggests that public drug programs should be identifying alternatives and including them on their formularies in a proactive manner, rather than reacting, often slowly, in the face of a shortage.

The committee therefore recommends that Health Canada, as a member of the Multi-Stakeholder Steering Committee on Drug Shortages, propose that non-primary care providers, such as dentists, be included as one of the stakeholders on the Multi-Stakeholder Steering Committee on Drug Shortages.

[Recommendation 23]

The committee further recommends that Health Canada amend the requirement in the *Food and Drug Regulations* regarding notification of drug discontinuance so as to provide longer notice when drugs are to be discontinued. [Recommendation 24]

¹⁸ Government of Canada, *Health Canada Seeks Input on Notification of Drug Shortages*, News Release, 22 May 2014.

¹⁹ Multi-Stakeholder Steering Committee on Drug Shortages, *Multi-Stakeholder Toolkit – A Toolkit for Improved Understanding and Transparency of Drug Shortage Response in Canada*, 2013, p. 22.



The committee further recommends that Health Canada request that the Multi-Stakeholder Steering Committee on Drug Shortages undertake a review of the drug shortages website to determine what modifications are necessary to address the concerns raised by stakeholders, related to timeliness of the information, usability, searchability, and the addition of other categories of information.

[Recommendation 25]

The committee further recommends that Health Canada urge the Multi-Stakeholder Steering Committee on Drug Shortages, through its Multi-Stakeholder Working Group, to fulfil its commitment to include clinical information about therapeutic alternatives on the drug shortages website within a year. [Recommendation 26]

The committee further recommends that the managers of public drug programs take action to include alternative therapeutics on their drug formularies that can be accessed in the event of a drug shortage. This includes,

- **the federal government’s drug programs for First Nations and Inuit, Veterans, Refugees, Armed Forces and federal inmates; and**
- **Health Canada, as a member of the Multi-Stakeholder Steering Committee on Drug Shortages, urging its provincial and territorial counterparts to incorporate therapeutic alternatives on their respective drug formularies.** [Recommendation 27]

IMPLEMENT POLICIES SPECIFIC TO ENVIRONMENTAL CONCERNS RELATED TO PRESCRIPTION DRUGS

There has to be a big public awareness around Take Back Programs.

— Janet Cooper, Canadian Pharmacists Association

Testimony from Environment Canada officials that there is no formal environmental surveillance for the presence of pharmaceutical contaminants came as something of a surprise to committee members. Committee members believe that there should be a formal program within Environment Canada to regularly monitor the environment, particularly freshwater bodies, for certain pharmaceuticals. Testimony from officials from the two departments that are supposed to share responsibility for this matter, Environment Canada and Health Canada, was unclear as to the role played by each department. For its part, a Health Canada representative deferred questions about environmental concerns to the Healthy Environments branch of the department. However, on a subsequent appearance by Health Canada officials, which included representatives from that branch, no clarifications were offered to the committee regarding Health Canada’s role.

The committee therefore recommends that the Minister of Health and the Minister of the Environment clarify the roles of their respective departments with respect to pharmaceutical contaminants in the environment, including but not limited to:

- **determining the list of pharmaceutical substances to be monitored in the environment;**
- **environmental sampling and testing of freshwater, groundwater, bio-solids, etc.;**
- **public reporting on the levels of pharmaceutical contaminants detected by surveillance; and,**
- **describing Health Canada's environmental assessment of approved drugs and how the information is used.** [Recommendation 28]

The committee therefore recommends that Health Canada, in consultation with stakeholders, develop and implement an aggressive public awareness campaign to encourage Canadians to take advantage of local Take Back programs and drop-off locations. [Recommendation 29]

The committee agrees that proper disposal of unused and expired medicine is one of the most important ways of reducing environmental exposure to these substances. It notes that Take Back programs (or, Drug Drop Off programs) not only reduce the amount of medicine in our sewers and landfills, but they also help to prevent diversion of potentially harmful drugs. Although a positive development has been the National Prescription Drug Drop-Off Day the committee would like to see a year-round focus on this important issue.

REDUCE THE RISKS ASSOCIATED WITH CONSUMPTION OF MULTIPLE PRESCRIPTION DRUGS

The polypharmacy issue is of major concern, particularly in the nursing home community.

— Brian O'Rourke, Canadian Agency for Drugs and Technologies in Health

The committee believes that implementation of the recommendations that it has put forward in its previous reports on post-approval monitoring and the off-label use of prescription drugs are critical





for addressing the issues associated with consuming multiple prescription drugs. Specifically, the Post-Approval Monitoring Report and the Off-Label Use Report recommended updating legislation and regulation; requiring long-term studies of drug safety; introducing facilitated and comprehensive adverse drug reaction reporting; conducting drug safety studies focussed on vulnerable sub-groups of the population; creating a broader mandate for the Drug Safety and Effectiveness Network; updating drug labelling to reflect new safety concerns; and improving communications strategies to relay those concerns to the public.

The committee supports and encourages the healthcare community in its development and dissemination of optimal prescribing practice guidelines. With respect to prescribing to patients who take multiple medications, or polypharmacy, the committee heard about the serious health consequences, particularly for the elderly. Members agree with the testimony of several witnesses that prescribers need guidelines to minimize the risks of overmedication and that prescribers should be encouraged to conduct regular medication reviews with these patients. While professional prescribing guidelines and medication reviews are necessary tools, education and on-going training, as emphasized by Emily Musing, a Board Member of the Canadian Patient

Safety Institute, are also critical to ensure that, ideally, patients consume only the number and amount of prescription medicines necessary to address their health concerns. These areas are currently under-represented in physician training programs and must be addressed immediately. The committee further urges the acceleration of the development of electronic medical and health records which will facilitate medication reviews by healthcare providers.

The committee therefore recommends that the Minister of Health encourage provincial and territorial Ministers of Health to ensure that medical students and health professionals receive sufficient training and continuing education on the issue of overmedication and the associated increased risk of adverse drug reactions. Programs should include the role of regularly updated optimal prescribing guidelines and patient medication reviews and should consider prescribing services that have been implemented in other countries. [Recommendation 30]



CONCLUSION

Once prescription drugs have obtained approval to be marketed in Canada, the drug regulator, Health Canada, still has a significant role to play. This role has been discussed in part in this committee's reports on post-approval monitoring for safety and effectiveness and off-label use. However, a number of unintended consequences relating to the use of prescription drugs also require the attention of Health Canada and the Public Health Agency of Canada. These issues include abuse, misuse and addiction; antibiotic resistance; counterfeit and substandard drugs; drug shortages; environmental concerns and the risks associated with overmedication.

Overall, more effort needs to be directed to the area of surveillance and data collection. Problems cannot be defined and solutions cannot be found without the proper information and statistics. This is the case for almost all issues addressed in this report, and the committee reiterates its call for

comprehensive implementation of electronic health and prescription drug databases. Awareness and education also became prominent themes during this study; Canadians should be alerted to and provided with information regarding the concerns raised in this report.

A number of recommendations within six areas of concern suggest that the Minister of Health and Health Canada take assertive action to protect the health of Canadians with respect to prescription drug abuse and addiction, counterfeit and substandard drugs and drug shortages. The committee calls on the Public Health Agency of Canada to increase its efforts in the area of antibiotic resistance. Finally, this committee calls on the Ministers of Health and Environment, and their respective departments, to work collaboratively to define their roles and establish activities with respect to addressing environmental concerns associated with prescription drugs.





APPENDIX A – LIST OF RECOMMENDATIONS

RECOMMENDATION 1

The committee therefore recommends that the Minister of Health—in conjunction with recommendations 9, 10 and 11 of the committee’s *Post-Approval Monitoring Report* regarding electronic medical records, electronic health records and provincial drug information systems, and with recommendation 1 of the committee’s *Off-label Report* regarding electronic prescribing—take an active role in working with the provincial and territorial governments to:

- Establish targets for the implementation of each electronic health and prescription drug system;
- Promote the use and accelerate uptake of these databases by health professionals through an aggressive targeted awareness campaign; and,
- Report publicly on the progress of implementing electronic health and prescription drug systems.

RECOMMENDATION 2

The committee therefore recommends that the Minister of Health urge provincial and territorial Ministers of Health to ensure access to anonymized health data by those agencies, institutes and researchers whose responsibilities require such access.

RECOMMENDATION 3

The committee therefore recommends that Health Canada post regular updates on its website regarding its progress towards expanding the National Anti-Drug Strategy to include prescription drug abuse.

RECOMMENDATION 4

The committee further recommends that the prevention component of the expanded National Anti-Drug Strategy require that;

- Health Canada develop and implement Canada-wide public awareness campaigns on the risks and harms of prescription drug abuse; and,
- The Minister of Health work with provincial and territorial Ministers of Health and stakeholders including the College of Family Physicians of Canada, the Royal College of Physicians and Surgeons of Canada, the Federation of Medical Regulatory Authorities of Canada and the Association of Faculties of Medicine of Canada, to optimize physician education and training regarding prescription drug abuse and addiction; and,
- The Minister of Health work with interested stakeholder groups to identify opportunities for pharmacist involvement.

RECOMMENDATION 5

The committee further recommends that ongoing discussions related to the expansion of the National Anti-Drug Strategy include negotiations with all jurisdictions to ensure access to data on prescription opioid use for those stakeholders involved in assessing the problem of prescription drug abuse.

RECOMMENDATION 6

The committee further recommends that Health Canada, through its representation on the Board of Directors at the Canadian Institute for Health Information (CIHI), urge that CIHI be mandated to track, and regularly report on, prescription drug use, particularly use of those drugs that have been identified as having a high potential for misuse, abuse and addiction based on information from provincial/territorial drug information systems.



RECOMMENDATION 7

The committee therefore recommends that Health Canada include a prescription drug's potential for addiction as part of the department's assessment of a drug's safety and effectiveness such that addictiveness is noted as one of the risks associated with using the drug.

RECOMMENDATION 8

The committee further recommends that Health Canada reassess the safety and efficacy profile of any approved drug that has a high potential for addiction.

RECOMMENDATION 9

The committee therefore recommends that, as a condition of market approval, all prescription opioids that have a potential for abuse be required to incorporate tamper-resistant technology in their design.

RECOMMENDATION 10

The committee further recommends that Health Canada extend the requirement for "Black Box" labelling noted in recommendation 17 of the committee's *Post-Approval Monitoring Report* to those drugs of high addictive potential.

RECOMMENDATION 11

The committee further recommends Health Canada implement requirements under the Narcotic Control Regulations:

- specifying the comprehensive information, including cautions regarding addiction and abuse potential, that must be provided to consumers by practitioners and pharmacists; and,
- restricting opioid prescriptions to the 200mg "watchful dose" identified in the Canadian Guideline for Safe and Effective Use of Opioids for Non-cancer Pain.

RECOMMENDATION 12

The committee therefore recommends that the expansion of the National Anti-Drug Strategy;

- Provide adequate and sustained funding for prescription drug addiction services for First Nations; and,
- Provide physicians serving First Nations' communities with culturally-sensitive pain management training, including the use of non-opioid options.

RECOMMENDATION 13

The committee further recommends that Health Canada's review of the Non-Insured Health Benefits program:

- include in its review of the drug formulary, a thorough assessment of all pain relievers, both prescription and non-prescription, with a view to encouraging the use of non-opioid alternatives wherever appropriate;
- include a requirement that tamper-resistant opioids be listed in preference to products without tamper-resistance;
- include an analysis of the current "limited use" status of Suboxone®; and,
- be completed and reported publicly on an urgent basis.

RECOMMENDATION 14

The committee therefore recommends that the Public Health Agency of Canada establish a multi-disciplinary, inter-agency group tasked with implementing a national action plan to address antibiotic resistance, as outlined by the Canadian Committee on Antibiotic Resistance in 2004. The action plan must include:

- a national public awareness campaign on the causes and consequences antibiotic resistance;



- renewed surveillance efforts, including a requirement that the Public Health Agency of Canada work with the provinces and territories to require that hospitals collect data and report on antibiotic use and the emergence of antibiotic-resistant bacteria; and,
- a mandate for the Public Health Agency of Canada to assemble, analyse and report publicly on these data, much like the model of the European Union.

RECOMMENDATION 15

The committee further recommends that the federal government:

- develop and implement a policy, in collaboration with and acknowledgment of the numerous parties involved, to ban or substantially reduce the use of antibiotics as growth promoters in food-producing animals; and,
- post regular updates on all relevant federal government websites on the progress of implementing its new policy which aims to reduce the use of antibiotics as growth promoters in food-producing animals.

RECOMMENDATION 16

The committee further recommends that the federal government encourage research into the development of new antibiotics in a variety of ways, including but not limited to:

- exploring incentives for the pharmaceutical industry such as extended market exclusivity, priority review and guidance on clinical trial design, to acknowledge the limited market for new antibiotics that would likely not be a first line therapy; and,
- creating a funding program specifically for antibiotic development at the Canadian Institutes of Health Research.

RECOMMENDATION 17

The committee therefore recommends that the Minister of Health consult with stakeholders and review the issue of Internet pharmacies operating in Canada that are selling unapproved medicines with a view to implementing the necessary changes, whether they be legislative, regulatory or other, so as to facilitate the successful prosecutions of these enterprises.

RECOMMENDATION 18

The committee further recommends that the Minister of Health, along with law enforcement and border security organizations, engage international counterparts in discussions to develop and enter into an international treaty to facilitate prosecutions for the counterfeiting of prescription drugs globally.

RECOMMENDATION 19

The committee further recommends that Health Canada implement a public awareness campaign warning of the risks of purchasing prescription drugs from online pharmacies.

RECOMMENDATION 20

The committee therefore recommends that the Minister of Health direct Health Canada to immediately develop and implement a new inspection policy for drug manufacturing sites which:

- mandates increased inspection activity by Health Canada, either alone or in collaboration with MRA partners, as well as the United States, of sites in countries whose regulatory system is not recognized by Health Canada as equivalent;
- prohibits the use of records as the only information used for inspections but rather requires that inspections involve on-site, physical examinations;



- requires public reporting on the results within one year of these site inspections; and,
- commits to reporting publicly any non-compliance issues detected by the inspection activities of drug regulators of other jurisdictions for sites for which a Canadian Drug Establishment Licence has been issued.

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The committee therefore recommends that the Minister of Health:

- establish an inter-agency task force which includes relevant representation from federal and provincial health and law enforcement agencies and the Canada Border Services Agency, to assess imported drugs, determine which types of drugs are most often counterfeited or not meeting GMP standards and determine the countries in which those drugs are being manufactured;
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- report publicly on the findings of the task force; and,
- determine the regulatory, inspection and enforcement actions necessary to address the issue of counterfeit and substandard medicines.

RECOMMENDATION 22

The committee further recommends that Health Canada:

- report publicly on its pilot program that randomly samples and tests medicines at the border using Raman Spectroscopy, including Health Canada's intentions as to whether to implement the use of the technology on a permanent basis; and,

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RECOMMENDATION 23

The committee therefore recommends that Health Canada, as a member of the Multi-Stakeholder Steering Committee on Drug Shortages, propose that non-primary care providers, such as dentists, be included as one of the stakeholders on the Multi-Stakeholder Steering Committee on Drug Shortages.

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- the federal government's drug programs for First Nations and Inuit, Veterans, Refugees, Armed Forces and federal inmates; and
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RECOMMENDATION 28

The committee therefore recommends that the Minister of Health and the Minister of the Environment clarify the roles of their respective departments with respect to pharmaceutical contaminants in the environment, including but not limited to:

- determining the list of pharmaceutical substances to be monitored in the environment;
- environmental sampling and testing of freshwater, groundwater, bio-solids, etc.;
- public reporting on the levels of pharmaceutical contaminants detected by surveillance; and,
- describing Health Canada's environmental assessment of approved drugs and how the information is used.

RECOMMENDATION 29

The committee therefore recommends that Health Canada, in consultation with stakeholders, develop and implement an aggressive public awareness campaign to encourage Canadians to take advantage of local Take Back programs and drop-off locations.

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APPENDIX B – WITNESSES

Wednesday, January 29, 2014

Canadian Patient Safety Institute	Hugh MacLeod, Chief Executive Officer Emily Musing, Board member
Health Council of Canada	Dr. Ingrid Sketris, Councillor

Thursday, January 30, 2014

Canadian Agency for Drugs and Technologies in Health	Brian O'Rourke, President and CEO
Canadian Institute for Health Information	John Wright, President and CEO Michael Gaucher, Director

Wednesday, February 5, 2014

Coalition on Prescription Drug Misuse	Susan Ulan, Co-chair
Canadian Centre on Substance Abuse	Robert Eves, Director, Strategic Partnerships & Knowledge Mobilization Paula Robeson, Knowledge Broker

Thursday, February 6, 2014

Centre for Addiction and Mental Health	Beth Sproule, Clinician Scientist, Pharmacy
Reckitt Benckiser Pharmaceuticals (Canada)	Cameron Bishop, Country Manager (Acting)

Wednesday, February 12, 2014

Alliance for the Prudent Use of Antibiotics	Dr. Scott McEwen, Professor, Department of Population Medicine, University of Guelph
Canadian Antimicrobial Resistance Alliance	Dr. Philippe Lagacé-Wiens, Medical Microbiologist, Department of medical microbiology and infectious diseases, University of Manitoba

Thursday, February 13, 2014

Alberta Health Services, Infection Prevention & Control (IPC)	Dr. John Conly, directeur, Foothills Medical Centre
BC Centre for Disease Control	Dr. David Patrick, Medical Epidemiology Lead for Antimicrobial Resistance



Wednesday, February 26, 2014

Canadian Association for Pharmacy Distribution Management	David Johnston, President and CEO
Canadian Dental Association	Dr. Gary MacDonald, President-elect Dr. Peter Doig, President
HealthPRO Procurement Services Inc.	Kathleen Boyle, Vice President, Pharmacy Services
Ontario Ministry of Health and Long-Term Care	Diane McArthur, Assistant Deputy Minister, Public Drug Programs Division

Thursday, February 27, 2014

Environment Canada	Karen Dodds, Assistant Deputy Minister, Science and Technology Branch Joanne Parrot, Chief, Bioassays and Toxicity Assessments
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Wednesday, March 5, 2014

Canada Border Services Agency	Martin Bolduc, Vice-president, Operations
Royal Canadian Mounted Police	Deputy Commissioner Mike Cabana, Federal Policing
As an individual	Amir Attaran, Canadian Research Chair, Population Health and Global Development Policy, University of Ottawa

Thursday, March 6, 2014

Canadian Generic Pharmaceutical Association	Jody Cox, Vice-president, Federal and International Affairs Dr. Colin D’Cunha, Director, Global Medical Affairs, Apotex Inc.
Rx&D	Walter Robinson, Vice President, Government Relations Jared Rhines, Vice-president, Scientific and Strategic Affairs

Wednesday, March 26, 2014

Canadian Pharmacists Association	Janet Cooper, Senior Director, Membership and Professional Affairs Phil Emberley, Director, Pharmacy Innovation
Federation of Medical Regulatory Authorities of Canada	Fleur-Ange Lefebvre, Executive Director and Chief Executive Officer
Canadian Medical Association	Owen Adams, Vice-president, Health Policy and Research Millicent Toombs, Director, Public Health Department



Thursday, March 27, 2014

Institute for Clinical Evaluative Sciences Dr. David Juurlink, Head, Division of clinical pharmacology and toxicology, Sunnybrook Health Sciences Centre

As an individual Michal Abrahamowicz, James McGill Professor, Department of Epidemiology, Biostatistics & Occupational Health, McGill University

Wednesday, April 2, 2014

Patients Canada Sholom Glouberman, President

PharmaWatch Canada Colleen Fuller, Chair

Thursday, April 3, 2014

As individuals Wendy Krkosek, Research Engineer, Centre for Water Resources Studies, Dalhousie University

Rebecca Klaper, Associate professor, School of Freshwater Sciences, University of Wisconsin-Milwaukee

Wednesday, April 9, 2014

Assembly of First Nations Stan Beardy, Regional Chief, Ontario

National Native Addictions Partnership Foundation Carol Hopkins, Executive Director

Thursday, April 10, 2014

Health Canada Dr. Supriya Sharma, Acting Associate Assistant Deputy Minister, Health Products and Food Branch

Robin Chiponski, Director General, Health Products and Food Branch

Canadian Institutes of Health Research Dr. Jane Aubin, Executive Vice-President, Chief Scientific Officer

Dr. Robert Peterson, Executive Director, Drug Safety and Effectiveness Network

Public Health Agency of Canada Dr. Theresa Tam, Branch Head, Health Security Infrastructure Canada



Wednesday, April 30, 2014

Health Canada

Dr. Supriya Sharma, Acting Associate Assistant
Deputy Minister, Health Products and Food Branch

Robin Chiponski, Director General, Health
Products and Food Branch Inspectorate

Barbara Moran, Director, Prescription Drug
Abuse Bureau, Controlled Substances and
Tobacco Directorate, Healthy Environments
and Consumer Safety Branch

John Worgan, Director, New Substances
Assessment and Control Bureau, Healthy
Environments and Consumer Safety Branch

Public Health Agency of Canada

Dr. Theresa Tam, Branch Head, Health
Security Infrastructure Branch





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