Spring 2015

Reports of the Auditor General of Canada

REPORT 1

Antimicrobial Resistance

OAG

Office of the Auditor General of Canada

Performance audit reports

This report presents the results of a performance audit conducted by the Office of the Auditor General of Canada under the authority of the *Auditor General Act*.

A performance audit is an independent, objective, and systematic assessment of how well government is managing its activities, responsibilities, and resources. Audit topics are selected based on their significance. While the Office may comment on policy implementation in a performance audit, it does not comment on the merits of a policy.

Performance audits are planned, performed, and reported in accordance with professional auditing standards and Office policies. They are conducted by qualified auditors who

- establish audit objectives and criteria for the assessment of performance,
- gather the evidence necessary to assess performance against the criteria,
- report both positive and negative findings,
- conclude against the established audit objectives, and
- make recommendations for improvement when there are significant differences between criteria and assessed performance.

Performance audits contribute to a public service that is ethical and effective and a government that is accountable to Parliament and Canadians.

The Report is available on our website at www.oag-bvg.gc.ca.

Ce document est également publié en français.

Cat. No. FA1-2015/1-1E-PDF
ISBN 978-1-100-25880-5
ISSN 1701-5413

Table of Contents

Introduction

Background

Antimicrobial resistance

1.1 **Antimicrobial drugs**, commonly called "antimicrobials," are considered a cornerstone of modern medicine. Health professionals rely on these drugs to treat common infections, such as pneumonia, and reduce the risk of serious complications and death.

1.2 Antimicrobials are also used to prevent infection. Using them allows health professionals to perform many medical procedures more safely, including organ transplants, joint replacements, and chemotherapy for cancer. Without effective antimicrobials to control the risk of infection, even routine surgeries, such as appendectomies, could lead to serious complications.

1.3 The effectiveness of antimicrobials has been declining due to the development of resistance. When an organism develops resistance to an antimicrobial drug, the drug is no longer effective for treating or preventing the infections caused by this organism. Resistance can happen with all types of antimicrobials; however, the World Health Organization considers resistance to antibiotics to be the most urgent concern. Antimicrobial resistance develops naturally, but it accelerates when antimicrobials are not used prudently—meaning the right drug used at the right dose, frequency, and duration.

1.4 Infections caused by organisms that have developed resistance may require lengthier and costlier treatments, some with serious side effects, and carry a higher risk of death for patients. For some multi-drug-resistant infections, few treatments are available. The World Health Organization considers seven organisms that cause common infections and have high rates of resistance to antibiotics to be of greatest concern:

- *Escherichia coli* (E. coli), a common cause of diarrhea, urinary tract infections, and bloodstream infections;
- *Klebsiella pneumoniae*, which can cause pneumonia, urinary tract infections, and bloodstream infections;
- *Staphylococcus aureus*, which can cause wound infections and bloodstream infections;

Antimicrobial drug—Defined by the Public Health Agency of Canada as a natural, semisynthetic, or synthetic substance that is capable of killing or inhibiting the growth of organisms. There are several types of these drugs, including antibiotics (effective against bacteria), antivirals, antifungals, and antiparasitics.

- *Streptococcus pneumoniae*, a cause of pneumonia, meningitis, and ear infections;
- non-typhoidal *Salmonella* organisms, which can cause diarrhea and bloodstream infections;
- *Neisseria gonorrhoeae*, which causes gonorrhea; and
- *Shigella* organisms, which can cause diarrhea.

In 2014, the World Health Organization reported that in many countries, more than half of the samples of most of these organisms were resistant to some of the antibiotics used to treat the infections they cause. It reported resistance rates from Canada ranging from 0 to 31 percent for the first six organisms. Infections caused by *Shigella* organisms are rare in Canada, and the drug resistance of these organisms is not tracked.

1.5 The Centers for Disease Control and Prevention estimated that there were two million cases of drug-resistant infections in the United States in 2013, contributing to around 23,000 deaths. Analyses from the European Centre for Disease Control have estimated that there are 25,000 deaths caused by some drug-resistant infections each year in Europe.

1.6 In Canada, available data from the Public Health Agency of Canada (the Agency) shows that the number of drug-resistant infections has been increasing. For example, the Agency's data indicates that infections in hospitalized patients that were caused by a drug-resistant form of *Staphylococcus aureus* increased nearly 20-fold from 1995 to 2005, but have levelled off since then. The Agency also estimates that 18,000 Canadians in hospitals contract drug-resistant infections each year, but it does not track all related deaths. Further, according to the Agency, almost one third of the cases of gonorrhea reported between 2008 and 2012 were resistant to at least one antimicrobial.

1.7 When antibiotics were first introduced, the health risks posed by the emergence of organisms resistant to antibiotics were largely mitigated by the development of new and effective drugs. This is no longer the case. Over the past 30 years, very few new antibiotics have been brought to market. According to the World Health Organization, many pharmaceutical companies have stopped developing antibiotics due to the high cost, long time frame, and perceived lack of financial return.

1.8 Since 1998, the World Health Organization has developed many recommendations to help countries put measures in place to control antimicrobial resistance. These include developing and implementing national plans to improve antimicrobial use in humans and animals, surveillance, and infection prevention and control, as well as to promote research and innovation.

Roles and responsibilities

1.9 In Canada, responsibilities related to antimicrobial use, surveillance, infection prevention and control, and research and innovation are shared among the federal, provincial, and territorial governments, as well as with professional organizations, private industry, and non-governmental organizations.

1.10 **Public Health Agency of Canada.** The Agency is responsible for coordinating national responses to public health threats and has identified antimicrobial resistance as such a threat. The Agency provides national leadership on the public health aspects of antimicrobial resistance and antimicrobial use. This includes developing guidelines and tools for antimicrobial-resistant infections, and conducting surveillance of antimicrobial-resistant organisms in humans and antimicrobial use in humans and animals.

1.11 **Health Canada.** Health Canada (the Department) is responsible for promoting and preserving the health of Canadians and for protecting them from risks to health and the spreading of diseases. With respect to antimicrobial resistance, the Department is responsible for approving antimicrobial drugs for sale in Canada and for promoting their prudent use in humans and animals. More specifically, the Department is responsible for monitoring the safety and effectiveness of approved antimicrobials and for ensuring that product labels provide up-to-date information on how these drugs should be used. The Department has no authority to control the use of human or veterinary drugs once they have been approved for sale.

Focus of the audit

1.12 This audit examined whether the Public Health Agency of Canada and Health Canada had fulfilled key responsibilities to mitigate the public health risks posed by the emergence and spread of antimicrobial resistance. The audit focused on antibiotic resistance.

1.13 We examined whether the Public Health Agency of Canada had engaged key partners in the development of a pan-Canadian strategy to address antimicrobial resistance and whether it had produced surveillance information to monitor the scope of antimicrobial resistance and antimicrobial use. We examined whether the Public Health Agency of Canada had issued guidelines to help prevent and control antimicrobial-resistant infections. We also examined whether Health Canada had taken steps in key areas to mitigate risks to human health posed by antimicrobial resistance by regulating the sale of antimicrobials and promoting prudent use of these drugs in humans and food animals.

1.14 The audit did not examine the surveillance of antimicrobial-resistant infections in animals or efforts to prevent and control these infections. Nor did our audit examine inspection programs to verify the quality of human and veterinary antimicrobials, or efforts to alleviate drug shortages or regulate antimicrobials in disinfectants, pesticides, or consumer products.

1.15 More details about the audit objective, scope, approach, and criteria are in **About the Audit** at the end of this report (see pages 20–22).

Findings, Recommendations, and Responses

Developing a pan-Canadian antimicrobial resistance strategy

Significant work to develop a pan-Canadian antimicrobial resistance strategy remains to be done

Overall finding

1.16 Overall, we found that the Public Health Agency of Canada (the Agency) has not succeeded in mobilizing all federal, provincial, and territorial partners and other stakeholders toward the development of a pan-Canadian strategy to address antimicrobial resistance. Since 2011, the Agency has discussed areas of collaboration with the provinces and territories, but has not succeeded in achieving consensus on the scope of such a strategy. In 2014, the Agency engaged with some federal organizations to develop a federal framework to address antimicrobial resistance. However, the Agency, in collaboration with its partners, has not yet determined how the framework will be used to mobilize the provinces, territories, and other stakeholders in identifying priority actions, clarifying roles and responsibilities, and establishing clear and realistic deadlines for the development of a pan-Canadian strategy.

1.17 This finding is important because there is no national strategy in place to address antimicrobial resistance. The Public Health Agency of Canada considers that dealing with this issue requires a comprehensive approach with strong national leadership and the cooperation of all levels of government and sectors. The Agency also considers that the lack of integration and coordination of activities raises the health risks posed by antimicrobial resistance.

1.18 Our analysis supporting this finding presents what we examined and discusses

- the Agency's commitment to a pan-Canadian strategy,
- development of a federal framework, and
- work remaining to develop a pan-Canadian strategy.

Context

1.19 Antimicrobial resistance is a global public health challenge. It affects human and animal health, agriculture, the environment, and the economy. Organisms resistant to antimicrobial drugs can emerge in humans, animals, or the environment. These organisms can be transmitted from animals to humans through food or direct contact. Drug-resistant organisms in the environment can be transmitted to humans and animals through water, for example.

1.20 The World Health Organization has pointed out that many of the factors that favour the emergence and spread of antimicrobial resistance, and the measures needed to combat it, are known. One such measure that the World Health Organization identified is to develop and implement a comprehensive national strategy that includes actions that help

- reduce antimicrobial use in humans and animals,
- improve surveillance,
- prevent and control the spread of drug-resistant infections, and
- stimulate research and innovation.

It has urged countries repeatedly since 2005 to develop such strategies. In May 2014, the Government of Canada endorsed a World Health Assembly resolution that called on member states to develop national strategies to combat antimicrobial resistance and facilitate international collaboration.

1.21 According to the World Health Organization, several countries have developed their own national strategies to address antimicrobial resistance, including Germany (in 2008), France (in 2011), the United Kingdom (in 2013), and the United States (in 2014). These strategies focus on reducing antibiotic use and preventing the emergence and spread of antibiotic resistance.

1.22 The Government of Canada has long been aware of the need for a national strategy. In 1997, Health Canada and the Canadian Infectious Disease Society (now the Association of Medical Microbiology and Infectious Disease Canada) convened a national conference that developed a national antimicrobial resistance strategy.

1.23 In 1998, the Government of Canada created the Canadian Committee on Antibiotic Resistance to coordinate national actions to control the development and spread of antimicrobial resistance. In 2004, the Committee published a revised national strategy.

1.24 From 2005 to 2009, the Agency provided around $900,000 to the Committee to implement elements of the national strategy and complete other activities. In 2009, the Agency stopped funding the Committee. The Agency and the Committee agreed that a more comprehensive approach with stronger national leadership was needed to effectively address antimicrobial resistance.

Recommendation

1.25 Our recommendation in this area of examination appears at paragraph 1.37.

Analysis to support this finding

1.26 **What we examined.** We examined whether the Public Health Agency of Canada had engaged key partners in the development of a pan-Canadian strategy to address antimicrobial resistance that would

- reduce antimicrobial use in humans and animals,
- improve surveillance of antimicrobial resistance and antimicrobial use,
- strengthen measures to prevent the emergence and spread of drug-resistant infections, and
- stimulate research and innovation.

1.27 When the Agency stopped funding the Canadian Committee on Antibiotic Resistance in 2009, it identified the need for a more comprehensive pan-Canadian strategy and for stronger national leadership. The Agency also noted that there was no provincial or territorial consensus on what the Agency's role should be on the issue of antimicrobial resistance.

1.28 **The Agency's commitment to a pan-Canadian strategy.** In 2011, the Agency identified antimicrobial resistance as one of the highest public health risks facing Canadians, along with mental illness, obesity, emerging infectious diseases, and the health of Aboriginal people and Northerners. It noted that the lack of integration and coordination of activities at the federal and national levels increased the risk that antimicrobial resistance would remain a threat to Canadians. The Agency committed to developing a pan-Canadian strategy to address antimicrobial resistance by mid-2015.

1.29 In April 2012, the Agency endorsed the development of a pan-Canadian strategy to reduce, limit, and control the emergence and spread of antimicrobial resistance. This multi-sectoral strategy would include all levels of government and sectors affected by the issue, including human health, animal health, agriculture, and industry. The strategy would focus on encouraging the appropriate use of antimicrobials; monitoring the emergence, spread, and impact of antimicrobial resistance; and increasing knowledge and developing tools to better address the issue. The Agency intended to lead the development of this strategy.

1.30 At the time, the Agency planned to engage with other federal organizations to identify opportunities to control the emergence and spread of antimicrobial resistance and gauge their interest in developing a multi-sectoral approach to do so. The Agency also planned to engage provinces, territories, and other stakeholders to discuss opportunities for collaboration. However, it did not establish clear deadlines for its engagement.

1.31 We found that the Agency did not engage with all federal, provincial, and territorial partners and other stakeholders from affected sectors as planned. It discussed areas for collaboration with its public health counterparts in the provinces and territories, but did not achieve consensus to pursue the development of a pan-Canadian strategy.

1.32 **Development of a federal framework.** In August 2013, the Agency decided to work more closely with other federal organizations. This was considered necessary to coordinate a federal approach to antimicrobial resistance. The Agency worked with Health Canada, the Canadian Food Inspection Agency, Agriculture and Agri-Food Canada, and the Canadian Institutes of Health Research to develop this approach.

1.33 The Minister of Health published *Antimicrobial Resistance and Use in Canada: A Federal Framework for Action* (the federal framework) in October 2014. It focuses on three areas:

- surveillance,
- promoting prudent antimicrobial use, and
- innovation.

The federal framework is intended to provide a cohesive and collaborative federal approach to address antimicrobial resistance. It is meant to serve as a starting point for engaging and mobilizing stakeholders from all sectors to address antimicrobial resistance. At the time of the audit, the Agency and its federal partners were developing an action plan to guide the implementation of the federal framework.

1.34 **Work remaining to develop a pan-Canadian strategy**. The federal framework emphasizes that provinces, territories, and other stakeholders play key roles in helping to address antimicrobial resistance. The Agency has recently sought input from its provincial and territorial public health counterparts on the potential scope of a pan-Canadian strategy for the health sector, but it does not know the extent to which they will participate. In addition, the Agency has not yet determined how other stakeholders will be involved. In fall 2014, the Agency created a committee of external experts to provide advice on this issue. In the agri-food sector, the Agency expects its federal partners to engage with provinces, territories, and other stakeholders. It has not yet been determined whether and how the health and agri-food sectors will work together.

1.35 The federal government first identified the need for a pan-Canadian strategy in 1997. In 2009, the Agency acknowledged that a more comprehensive approach with stronger national leadership was needed. Although efforts have been made to mobilize partners toward the development of such a strategy, significant work remains to be done.

1.36 In our opinion, it is likely that the development of a pan-Canadian strategy will take many years, given that, according to the Agency, such a strategy requires the cooperation of all levels of government and sectors.

1.37 **Recommendation.** The Public Health Agency of Canada, in cooperation with its federal partners, provinces, territories, and other stakeholders, should identify priority actions, clarify roles and responsibilities, and establish clear and realistic deadlines for the development of a pan-Canadian strategy to address antimicrobial resistance.

The Agency's response. *Agreed. The Public Health Agency of Canada will work in collaboration with its federal partners, provinces, territories, and other stakeholders implicated in antimicrobial resistance (including the public health, health care, animal health, and agri-food sectors) to identify priority actions, to clarify roles and responsibilities, and to establish deadlines for the development of a pan-Canadian strategy.*

Tackling the complex issue of antimicrobial resistance and use requires a concerted and coordinated effort from all levels of government and the health care, animal health, agricultural, and pharmaceutical sectors. The Government of Canada's Antimicrobial Resistance and Use in Canada: A Federal Framework for Action *and a related action plan describe the government's role and priority actions on antimicrobial resistance and use.*

Surveillance of antimicrobial resistance and use

The Public Health Agency of Canada is developing a strategy to address surveillance weaknesses

Overall finding ➔

1.38 Overall, we found that the Public Health Agency of Canada (the Agency) has identified weaknesses in its collection, analysis, and dissemination of surveillance information on antimicrobial resistance and antimicrobial use. The Agency is developing a strategy to address these weaknesses, but has yet to finalize the scope of improvements, funding sources, and timelines for implementation.

1.39 This finding is important because the Public Health Agency of Canada is responsible for obtaining, analyzing, and disseminating national-level surveillance information about antimicrobial resistance and antimicrobial use. This information is needed to understand the scope of resistance and the extent of antimicrobial use in Canada. Based on this understanding, actions can be taken to mitigate the risks to human health.

1.40 Our analysis supporting this finding presents what we examined and discusses the Agency's

- collection and analysis of information,
- integration of information,
- timeliness of reporting, and
- corrective actions.

Context

1.41 Public health surveillance involves the continuous and systematic collection, analysis, and interpretation of health-related data. Surveillance can provide early warnings to support timely public health interventions and inform effective health programs, guidelines, and policies.

1.42 According to the Agency, national surveillance data is needed to monitor trends in antimicrobial-resistant organisms and antimicrobial use. This information is used to inform policy and public health actions, and provides a baseline for measuring the effectiveness of interventions.

1.43 The Agency leads national surveillance efforts on antimicrobial resistance. To collect information, it relies on a network of partnerships with other federal departments and agencies, provinces and territories, hospitals, and private industry.

1.44 Surveillance information is collected and analyzed, and the results are made available on the Agency's website:

- The Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) collects information on a limited number of drug-resistant foodborne organisms from farms, abattoirs, retail meat, and humans. CIPARS also tracks some information about the use of antimicrobials in animals and humans. The information is used for several purposes, such as Health Canada's assessments of veterinary antimicrobial drugs.
- The Canadian Nosocomial Infection Surveillance Program provides data on a limited number of drug-resistant organisms from 59 large hospitals in Canada. Reports generated by the system highlight the resistance rates and trends of the organisms being monitored, which can be used to inform infection control measures.

The Agency also collects data on resistance trends in a limited number of organisms that cause diseases present in the community, such as tuberculosis and gonorrhea.

1.45 Given the important role that surveillance information plays in determining the scope of the risks posed by antimicrobial resistance, the World Health Organization has repeatedly urged member states to strengthen their surveillance capacities, most recently in 2011 and 2014. The Agency committed to improving its surveillance information in 2012 and has included this as a key component of the federal framework in 2014.

Recommendation

1.46 Our recommendation in this area of examination appears at paragraph 1.53.

Analysis to support this finding

1.47 **What we examined.** We examined whether the Agency had obtained, analyzed, and disseminated surveillance information to monitor the scope of drug-resistant organisms in Canada and the amount of antimicrobials being used in humans and animals. We also examined whether the Agency had taken steps to address any weaknesses it had identified.

1.48 **Collection and analysis of information.** In April 2014, the Agency reviewed its antimicrobial-resistance surveillance activities. We found that the Agency identified several weaknesses related to its surveillance information. For example:

- The Agency needs to obtain data on other organisms present in hospitals and in the food chain.
- The information that the Agency collects on drug-resistant infections that are detected and treated in community settings, such as clinics and long-term care facilities, is very limited. There is also a lack of data available on the extent of antimicrobial resistance in remote regions and in specific vulnerable populations, including Aboriginal peoples.
- The information that the Agency obtains on antimicrobial use in humans is insufficient. The Agency buys information on antimicrobial use in humans from a private company. This information details the prescriptions dispensed by a sample of community pharmacies, the antimicrobials purchased by hospitals, and the physicians' reasons for prescribing these antimicrobials. However, there is a need to obtain more information on usage in the health-care sector and in remote populations, including Aboriginal peoples.
- The information that the Agency obtains on antimicrobial use in animals is limited. It collects sales data; however, this does not include any veterinary antimicrobials that are directly imported for food animals (as further detailed in paragraphs 1.87 to 1.92). It also collects limited information about how and why antimicrobials are used in animals.

1.49 These weaknesses limit the Agency's ability to monitor the emergence and spread of drug-resistant organisms, measure antimicrobial use, and analyze the impact of antimicrobial-resistant infections in Canada. For example, it cannot analyze the additional health-care costs attributable to antimicrobial resistance. The Agency has noted that obtaining additional surveillance information would improve its capacity to conduct analysis and, over time, to assess the effectiveness of public health interventions.

1.50 **Integration of information.** The Agency has also highlighted a need to better integrate its surveillance information. It currently publishes its surveillance information in several separate reports. An integrated report

would provide a more complete picture of the extent of antimicrobial resistance in Canada. This would allow federal and provincial policy makers to compare the relative risks of various drug-resistant organisms in different settings and use this information to guide their decision making.

1.51 **Timeliness of reporting.** The Agency has identified a need for timelier reporting of surveillance information. It has taken some steps to improve its timeliness, such as introducing summary reports of its hospital surveillance information and streamlining its reporting of foodborne drug-resistant organisms.

1.52 **Corrective actions.** At the time of our audit, the Agency was developing an internal strategy to address the surveillance weaknesses it had identified. However, this strategy was still in draft form. Important aspects of its scope, funding, and time frame for implementation were not yet determined. The Agency plans to incorporate elements of this strategy into the action plan it is developing to implement the federal framework. It has noted that making the needed improvements to surveillance would require the collaboration of other federal departments and agencies, provinces and territories, professional associations, and other stakeholders.

1.53 **Recommendation.** The Public Health Agency of Canada, in collaboration with provinces, territories, and other health stakeholders, should finalize its strategy to address the weaknesses in surveillance it has identified to ensure that adequate data on antimicrobial resistance is available.

The Agency's response. *Agreed. The Public Health Agency of Canada will collaborate with provinces, territories, and other stakeholders who gather information to ensure that Canada has a comprehensive antimicrobial resistance surveillance system that provides timely and accurate data for decision makers.*

Building on Canada's current surveillance systems, the Canadian Antimicrobial Resistance Surveillance System (CARSS), planned to be created in April 2015, will provide an overall, integrated picture of antimicrobial resistance and use in Canada. CARSS will provide decision makers with information to guide their policies and actions. CARSS will look to integrate even more data sources as they become available.

Prudent antimicrobial use

Overall finding ➔

1.54 Overall, we found that the Public Health Agency of Canada (the Agency) and Health Canada (the Department) have taken some steps to promote prudent antimicrobial use in humans. The Agency has developed six national guidelines intended to prevent and control antimicrobial-resistant infections, but it has identified the need for

more. The Department requires that most antimicrobial drugs used in humans be sold by prescription only.

1.55 However, Health Canada has not taken some important steps needed to promote prudent antimicrobial use in food animals. For example, the Department has not strengthened existing regulations to prohibit farmers from importing unlicensed non-prescription antimicrobial drugs that are important to human medicine for use in their own animals. The Department does not assess these drugs for quality, safety, or efficacy. According to the Department, the use of these drugs in food animals may have serious public health implications, including the development of antimicrobial resistance. Furthermore, the Department allows certain antimicrobials that are used to treat serious infections in humans to be sold without a prescription for use in food animals.

Context

1.56 The World Health Organization has recommended that prudent use of antimicrobial drugs in humans and animals be encouraged through a variety of mechanisms, including public awareness campaigns, the development of guidelines, and the regulation of these drugs. Using antimicrobials prudently—that is, using the right drug at the right dose, frequency, and duration—to treat infections in humans and animals ensures that these infections are treated effectively while minimizing the risk that resistance will emerge.

1.57 Health Canada, as the regulator of human and veterinary drugs, is responsible for approving antimicrobial drugs for sale and ensuring that up-to-date information is available about how these drugs should be used. The Public Health Agency of Canada can promote prudent use by developing guidance for human health professionals and raising awareness of antimicrobial resistance. The provinces and territories, as well as human and animal health professionals, control the use of antimicrobials.

The Public Health Agency of Canada and Health Canada have taken some steps to promote prudent antimicrobial use in humans

What we found

1.58 We found that the Agency and the Department have taken steps intended to limit the emergence and spread of drug-resistant infections and to promote prudent antimicrobial use in humans. The Agency has developed guidelines for health professionals intended to prevent and control the emergence and spread of some antimicrobial-resistant infections, but has identified the need for more. Health Canada requires that most antimicrobials for use in humans be available only by prescription. However, the Department does not require that all antimicrobial drug labels include warnings to encourage prudent use.

1.59 Our analysis supporting this finding presents what we examined and discusses

- guidelines for health professionals,
- raising public awareness, and
- regulating the sale of antimicrobials for human use.

Why this finding matters

1.60 This finding is important because, according to the World Health Organization, providing guidelines and tools and making drugs available only by prescription helps to promote prudent antimicrobial use. Prudent use of antimicrobials helps prevent the emergence and spread of resistance and prolong the effectiveness of these drugs.

Recommendations

1.61 We made no recommendations in this area of examination.

Analysis to support this finding

1.62 **What we examined**. We examined whether the Agency, in partnership with others, had developed and disseminated guidelines and tools to help prevent and control drug-resistant infections. We also examined whether Health Canada had taken steps in key areas to mitigate the human health risks posed by antimicrobial resistance by regulating the sale of antimicrobial drugs and by promoting prudent use of these drugs in humans.

1.63 **Guidelines for health professionals.** One of the ways to prevent and control the emergence and spread of antimicrobial resistance is to develop and disseminate guidelines for use by health professionals. In Canada, provinces and territories produce many guidelines and other tools for their jurisdictions, while the Agency produces national guidelines that are intended to complement provincial and territorial guidelines.

1.64 The Agency consults with the provinces and territories to determine which national guidelines are needed. It brings together experts from across the country to develop national guidelines and other tools to help prevent and control infectious diseases, including some that are resistant to antimicrobials.

1.65 The Agency has developed a national guideline on routine infection-control practices that includes advice for managing the spread of infectious diseases, some of which are resistant to antimicrobials. It has also developed five national guidelines designed to limit the emergence and spread of specific antimicrobial-resistant infections. Two of these guidelines include treatment recommendations designed to prevent further emergence of resistance in the organisms that cause these infections.

1.66 In 2012, the Agency identified the need for another six guidelines for specific antimicrobial-resistant infections. However, it has placed the development of these guidelines on hold. The Agency refers Canadian

health professionals to other guidelines, such as those developed jointly by Alberta and British Columbia, to obtain the latest information on the use of antimicrobials.

1.67 **Raising public awareness**. Since 2010, the Agency has supported antimicrobial-resistance awareness campaigns led by stakeholder groups, including the Association of Medical Microbiology and Infectious Disease Canada. In 2013, the Agency committed to further increasing awareness. It launched a national campaign in November 2014. The campaign provided some information and tools for health professionals and the public to improve their understanding of antimicrobial resistance and what they can do to prevent it—for example, taking measures to limit the spread of infections and using antimicrobials more prudently. This campaign was a pilot project with one-time funding. The Agency plans to evaluate its results in spring 2015.

1.68 **Regulating the sale of antimicrobials for human use.** Health Canada has the authority to determine which antimicrobials are available by prescription only and which are available over the counter. The World Health Organization has recommended that all antimicrobial drugs for human use be available by prescription only. Health Canada has made most antimicrobials used in human medicine available by prescription only. However, some antimicrobials remain available over the counter. These are mostly products that are used topically, such as eye drops and skin creams. Health Canada officials told us they were not aware of such use increasing the risk of resistance developing.

1.69 Health Canada is also responsible for ensuring that labels for antimicrobial drugs provide information on how these drugs can be used prudently. The Department has developed standard warnings to encourage prudent use of antimicrobials in humans. Health Canada officials told us that these warnings are sometimes included when a new product is approved or when the labels for existing products are revised for other reasons. However, the Department does not require that products carry them. Health Canada does not plan to systematically review existing product labels and add such warnings.

Health Canada has not taken some important steps to promote prudent use of antimicrobials in food animals

What we found

1.70 We found that Health Canada has not taken some important steps to promote prudent use of antimicrobials in food animals to protect the effectiveness of antimicrobials important to human medicine. The Department allows certain antimicrobials important to human medicine to be sold without a prescription for use in food animals, and has not strengthened its control over the importation of unlicensed veterinary antimicrobials.

1.71 Our analysis supporting this finding presents what we examined and discusses

- assessing antimicrobial resistance risks,
- strengthening veterinary oversight,
- addressing the non-therapeutic use of antimicrobials important to human medicine, and
- controlling the importation of antimicrobials for use in food animals.

Why this finding matters

1.72 This finding is important because many of the antimicrobials used in food animals are also used to treat serious infections in humans. While antimicrobials are important for treating and preventing infections in food animals, imprudent use of them can lead to the development in animals of antimicrobial-resistant organisms that can spread to humans.

Recommendations

1.73 Our recommendations in this area of examination appear at paragraphs 1.93 and 1.94.

Analysis to support this finding

1.74 **What we examined.** The audit examined whether Health Canada had taken steps in key areas to mitigate risks to human health posed by antimicrobial resistance by regulating the sale of antimicrobials and by promoting prudent use of these drugs in food animals. More specifically, we examined whether Health Canada had

- considered risks related to the emergence of antimicrobial resistance before approving new antimicrobial products or before approving new uses for previously approved products;
- strengthened veterinary oversight of antimicrobials important to human medicine;
- terminated the approved use of antimicrobials for non-therapeutic purposes, such as growth promotion; and
- assessed whether its regulatory framework provides adequate control over the importation of veterinary antimicrobial drugs.

1.75 **Assessing antimicrobial resistance risks.** Health Canada is responsible for ensuring that all veterinary drugs approved for sale in Canada pose no risks to human health. Since 2004, the Department's veterinary drug review process has included a step to assess if there is a risk that an approved use of an antimicrobial important to human medicine might lead to the emergence of antimicrobial resistance. This assessment is supported by Health Canada's categorization of antimicrobials important to human medicine (Exhibit 1.1). In 2005, the Department identified a need to assess this risk for antimicrobials that had been approved before 2004.

Exhibit 1.1 Health Canada has categorized antimicrobials important to human medicine

There are three categories of antimicrobials important to human medicine.

- **Category I**—Antimicrobials of very high importance that are used to treat serious infections and for which there are limited or no treatment alternatives.
- **Category II**—Antimicrobials of high importance that are used to treat a variety of infections, including serious infections, and for which there are treatment alternatives.
- **Category III**—Antimicrobials of medium importance that are used to treat less serious infections and for which there are treatment alternatives.

Source: Adapted from Health Canada's Categorization of Antimicrobial Drugs Based on Importance in Human Medicine, 2009

1.76 According to Health Canada, there are four Category I antimicrobials approved for use in food animals. The Department has assessed risks related to the emergence of resistance to these antimicrobials. After assessing these risks, Health Canada implemented risk management measures for products containing these antimicrobials. This included adding antimicrobial-resistance warning statements to product labels, requesting that a manufacturer remove an approved use of one product, and taking steps to change the status of one antimicrobial from over the counter to prescription only.

1.77 To date, the Department has not assessed several Category II and Category III antimicrobials. Some of these antimicrobials are available over the counter and include non-therapeutic uses, such as growth promotion, among their approved uses.

1.78 **Strengthening veterinary oversight.** Health Canada has acknowledged that the involvement of veterinarians in decisions to treat food animals with antimicrobials is necessary for promoting prudent antimicrobial use. The Department has the administrative authority to require that antimicrobials important to human medicine be made available for use in food animals by prescription only.

1.79 Health Canada has taken steps to ensure that all Category I antimicrobials approved for use in food animals are sold by prescription only. However, it allows several Category II antimicrobials to be sold for use in food animals without a prescription. These antimicrobials are used to treat serious infections in humans. Since 2004, the Department has not authorized the over-the-counter sale of any new antimicrobial important to human medicine for use in food animals. Health Canada is also working with partners to develop options to strengthen veterinary oversight of antimicrobials important to human medicine.

1.80 Quebec and Newfoundland and Labrador have strengthened veterinary oversight of antimicrobial use beyond Health Canada's requirements. Quebec requires that all antimicrobials used in food animals be sold by prescription only. Newfoundland and Labrador also requires this, but makes an exception for antimicrobials approved for use in animal feed.

1.81 We also note that several other countries, including Norway, Denmark, the Netherlands, Sweden, and the United Kingdom, require that antimicrobials approved for use in animals be available only by prescription.

1.82 The development of a pan-Canadian strategy that includes the provinces and territories and key stakeholders from the agriculture and animal health sectors may provide Health Canada with an opportunity to strengthen veterinary oversight of antimicrobial use in food animals and ensure a more consistent approach to such use across the country.

1.83 **Addressing the non-therapeutic use of antimicrobials important to human medicine.** Health Canada has acknowledged that antimicrobials important to human medicine should not be used for non-therapeutic purposes, such as for promoting the growth of food animals. In 2006, the European Union fully implemented a ban on the use of antibiotics for growth-promotion purposes. The United States is working with industry to voluntarily prohibit this use and expects to complete this process by the end of 2016.

1.84 In 2007, Health Canada tried to address this issue by asking manufacturers of antimicrobials approved for growth-promotion purposes to support this use with better evidence of efficacy. For some products, the absence of such evidence was acknowledged and the authorization to use the product as a growth promoter was withdrawn.

1.85 However, about 20 percent of the approximately 330 antimicrobial products that contain Category II or III antimicrobials still include growth promotion among their approved uses. According to Health Canada, no products containing Category I antimicrobials are approved for growth-promotion purposes.

1.86 In April 2014, the Department announced its intention to again work with industry to remove growth-promotion claims for all antimicrobials important to human medicine by the end of 2016. It has developed an action plan with specific actions and timelines to undertake this work.

1.87 **Controlling the importation of antimicrobials for use in food animals.** Health Canada is aware that regulations presently do not prohibit the importation of non-prescription antimicrobial drugs important to human medicine that have not been licensed for sale in Canada, on the condition that these drugs will not be resold. As a result, farmers are able to import these drugs and use them in their own animals. This is often referred to as "own-use importation."

1.88 The Department is also aware that there are few regulatory controls over the importation of veterinary **active pharmaceutical ingredients**—including ingredients used in antimicrobial drugs important to human medicine. Health Canada has concerns about the importation and direct use of these ingredients in food animals.

1.89 Health Canada does not assess unlicensed antimicrobial drugs and active pharmaceutical ingredients brought into Canada through own-use importation for quality, safety, or efficacy. According to the Department, the use of these antimicrobials in food-producing animals may have serious public health implications, including the development of antimicrobial resistance. Health Canada also has limited information about the volume and type of antimicrobials imported for own-use and where they are imported from.

1.90 In 2002, the Department's Advisory Committee on Animal Uses of Antimicrobials and Impact on Resistance and Human Health recommended that Health Canada stop the importation of unlicensed veterinary antimicrobials and strengthen its control over the importation of veterinary active pharmaceutical ingredients. Health Canada has not done so. The Department has policies intended to limit own-use importation of veterinary drugs and to control the importation of veterinary active pharmaceutical ingredients. However, it acknowledges that regulatory amendments are needed to address these importation practices and the risks they pose to the emergence and spread of antimicrobial resistance.

1.91 In 2013, Health Canada held discussions with stakeholders to obtain their support for a new regulatory framework for veterinary drugs. Proposed regulatory changes that were discussed included prohibiting the own-use importation of antimicrobials important to human medicine and limiting the importation of veterinary active pharmaceutical ingredients to entities licensed by Health Canada.

1.92 The long-standing issue of own-use importation and the lack of control over the importation of veterinary antimicrobial active pharmaceutical ingredients may undermine national efforts to promote the prudent use of antimicrobials and limit the emergence and spread of antimicrobial resistance.

1.93 **Recommendation.** Health Canada should finalize its plans to address "own-use importation" of veterinary antimicrobial drugs and strengthen its control over the importation of veterinary antimicrobial active pharmaceutical ingredients.

Active pharmaceutical ingredient—An active ingredient that is used in the fabrication of a pharmaceutical.
Source: *Food and Drug Regulations*

The Department's response. *Agreed. Health Canada will implement measures to address the own-use importation of veterinary drugs and strengthen its control over the importation of veterinary active pharmaceutical ingredients. Health Canada will consult with stakeholders in developing measures to address oversight on importation.*

1.94 **Recommendation.** Health Canada should periodically review all antimicrobials important to human medicine to determine whether their approved uses and availability in veterinary medicine increase the risk that these antimicrobials will become ineffective in treating infections in humans.

The Department's response. *Agreed. Health Canada will proceed with an international benchmarking of post-market periodic review approaches. Health Canada will also develop a risk-based approach to periodic safety reviews while building on the new post-market authorities of the* Protecting Canadians from Unsafe Drugs Act *(Vanessa's Law). Health Canada will consult with stakeholders in developing approaches to periodic safety reviews.*

Conclusion

1.95 We concluded that the Public Health Agency of Canada (the Agency) and Health Canada (the Department) have not fulfilled key responsibilities to mitigate the public health risks posed by the emergence and spread of antimicrobial resistance in Canada.

1.96 Over the past five years, the Agency has discussed areas of collaboration with the provinces and territories, but has not succeeded in achieving consensus on the scope of a pan-Canadian strategy to address antimicrobial resistance. In 2014, the Agency engaged with some federal organizations to develop a federal antimicrobial resistance framework. The Agency has not determined how it will address the weaknesses it has identified in its collection, analysis, and dissemination of surveillance information on antimicrobial resistance and antimicrobial use. The Agency has taken some steps to promote prudent antimicrobial use in humans, such as developing and disseminating guidelines for health professionals, but has identified the need for more guidelines.

1.97 Health Canada has not taken some important steps to promote the prudent use of antimicrobials in food animals to protect the effectiveness of antimicrobials important to human medicine. For example, the Department allows certain antimicrobials used to treat serious infections in humans to be sold without a prescription for use in food animals. However, Health Canada has promoted prudent antimicrobial use in food animals by assessing risks related to the emergence of antimicrobial resistance as part of its veterinary drug review process. The Department promotes prudent antimicrobial use by making most antimicrobials for human use available only by prescription.

About the Audit

The Office of the Auditor General's responsibility was to conduct an independent examination of the responsibilities of the Public Health Agency of Canada (the Agency) and Health Canada (the Department) for addressing the emergence and spread of antimicrobial resistance, to provide objective information, advice, and assurance to assist Parliament in its scrutiny of the government's management of resources and programs.

All of the audit work in this report was conducted in accordance with the standards for assurance engagements set out by the Chartered Professional Accountants of Canada (CPA) in the CPA Canada Handbook—Assurance. While the Office adopts these standards as the minimum requirement for our audits, we also draw upon the standards and practices of other disciplines.

As part of our regular audit process, we obtained management's confirmation that the findings in this report are factually based.

Objective

The audit objective was to determine whether the Public Health Agency of Canada and Health Canada fulfilled key responsibilities to mitigate the public health risks posed by the emergence and spread of antimicrobial resistance in Canada.

Scope and approach

We examined whether the Public Health Agency of Canada had engaged key partners in the development of a pan-Canadian strategy to address antimicrobial resistance. We also examined whether it had obtained, analyzed, and disseminated surveillance information to monitor the scope of antimicrobial resistance and antimicrobial use. We examined whether the Agency had developed and disseminated guidelines and tools to help prevent and control antibiotic-resistant infections, including whether it worked to increase awareness of antimicrobial resistance among health-care professionals and the public. We also examined whether Health Canada had taken steps in key areas to mitigate risks to human health posed by antimicrobial resistance by regulating the sale of antimicrobials and by promoting prudent use of these drugs in humans and food animals.

Our audit did not examine the surveillance of antimicrobial-resistant infections in animals, and it did not examine efforts to prevent and control these infections. Our audit did not examine inspection programs to verify the quality of human and veterinary antimicrobials, and it did not examine efforts to alleviate drug shortages or to regulate antimicrobials in disinfectants, pesticides, or consumer products.

The audit approach included an examination of policies and documents related to the Agency's planning and engagement with stakeholders in the development of a pan-Canadian approach, including activities conducted through interdepartmental and intergovernmental forums. It also included a review of documentation related to the Agency's surveillance, guidance development, and public awareness activities, as well as interviews with Agency representatives. We also interviewed Health Canada representatives and examined policies and documentation related to the Department's regulation of human and veterinary antimicrobials.

Criteria

Criteria	Sources
To determine whether the Public Health Agency of Canada and Health Canada fulfilled key responsibilities to mitigate the public health risks posed by the emergence and spread of antimicrobial resistance in Canada, we used the following criteria:	
The Public Health Agency of Canada engages key partners toward the development of a coordinated pan-Canadian approach to address antimicrobial resistance.	• *Public Health Agency of Canada Act* • 2011–12 Report on Plans and Priorities, Public Health Agency of Canada • The World Health Organization's Policy Package to Combat Antimicrobial Resistance • World Health Assembly Resolution 58.27, 58th World Health Assembly, 2005 • World Health Assembly Resolution 67.25, 67th World Health Assembly, 2014
The Public Health Agency of Canada obtains, analyzes, and disseminates surveillance information to mitigate the human health risks posed by the emergence and spread of antimicrobial resistance.	• *Public Health Agency of Canada Act* • 2012–13 Report on Plans and Priorities, Public Health Agency of Canada • The World Health Organization's Policy Package to Combat Antimicrobial Resistance • World Health Assembly Resolution 58.27, 58th World Health Assembly, 2005 • World Health Assembly Resolution 67.25, 67th World Health Assembly, 2014
The Public Health Agency of Canada, in partnership with others, develops and disseminates national guidelines and tools for the prevention and control of infectious diseases with significant antimicrobial resistance.	• *Public Health Agency of Canada Act* • 2014–15 Report on Plans and Priorities, Public Health Agency of Canada • The World Health Organization's Policy Package to Combat Antimicrobial Resistance
Health Canada mitigates risks to human health from antimicrobial resistance by regulating the sale of antimicrobial drugs and by promoting their prudent use in humans and animals.	• *Food and Drugs Act* • The World Health Organization's Policy Package to Combat Antimicrobial Resistance • Terrestrial Animal Health Code, World Organization for Animal Health, 2013

Management reviewed and accepted the suitability of the criteria used in the audit.

Period covered by the audit

The audit covered the period between January 2011 and October 2014. Audit work for this report was completed on 19 December 2014.

Audit team

Assistant Auditor General: Ronnie Campbell
Principal: Michelle Salvail
Director: André Côté

Sébastien Bureau
Mark Carroll
Lisa Harris

List of Recommendations

The following is a list of recommendations found in this report. The number in front of the recommendation indicates the paragraph where it appears in the report. The numbers in parentheses indicate the paragraphs where the topic is discussed.

Recommendation	Response
Developing a pan-Canadian antimicrobial resistance strategy	
1.37 The Public Health Agency of Canada, in cooperation with its federal partners, provinces, territories, and other stakeholders, should identify priority actions, clarify roles and responsibilities, and establish clear and realistic deadlines for the development of a pan-Canadian strategy to address antimicrobial resistance. **(1.26–1.36)**	**The Agency's response.** Agreed. The Public Health Agency of Canada will work in collaboration with its federal partners, provinces, territories, and other stakeholders implicated in antimicrobial resistance (including the public health, health care, animal health, and agri-food sectors) to identify priority actions, to clarify roles and responsibilities, and to establish deadlines for the development of a pan-Canadian strategy. Tackling the complex issue of antimicrobial resistance and use requires a concerted and coordinated effort from all levels of government and the health care, animal health, agricultural, and pharmaceutical sectors. The Government of Canada's *Antimicrobial Resistance and Use in Canada: A Federal Framework for Action* and a related action plan describe the government's role and priority actions on antimicrobial resistance and use.
Surveillance of antimicrobial resistance and use	
1.53 The Public Health Agency of Canada, in collaboration with provinces, territories, and other health stakeholders, should finalize its strategy to address the weaknesses in surveillance it has identified to ensure that adequate data on antimicrobial resistance is available. **(1.47–1.52)**	**The Agency's response.** Agreed. The Public Health Agency of Canada will collaborate with provinces, territories, and other stakeholders who gather information to ensure that Canada has a comprehensive antimicrobial resistance surveillance system that provides timely and accurate data for decision makers. Building on Canada's current surveillance systems, the Canadian Antimicrobial Resistance Surveillance System (CARSS), planned to be created in April 2015, will provide an overall, integrated picture of antimicrobial resistance and use in Canada. CARSS will provide decision makers with information to guide their policies and actions. CARSS will look to integrate even more data sources as they become available.
Prudent antimicrobial use	
1.93 Health Canada should finalize its plans to address "own-use importation" of veterinary antimicrobial drugs and strengthen its control over the importation of veterinary antimicrobial active pharmaceutical ingredients. **(1.70–1.92)**	**The Department's response.** Agreed. Health Canada will implement measures to address the own-use importation of veterinary drugs and strengthen its control over the importation of veterinary active pharmaceutical ingredients. Health Canada will consult with stakeholders in developing measures to address oversight on importation.

Recommendation	Response
1.94 Health Canada should periodically review all antimicrobials important to human medicine to determine whether their approved uses and availability in veterinary medicine increase the risk that these antimicrobials will become ineffective in treating infections in humans. **(1.70–1.92)**	**The Department's response.** Agreed. Health Canada will proceed with an international benchmarking of post-market periodic review approaches. Health Canada will also develop a risk-based approach to periodic safety reviews while building on the new post-market authorities of the *Protecting Canadians from Unsafe Drugs Act* (Vanessa's Law). Health Canada will consult with stakeholders in developing approaches to periodic safety reviews.