Health Canada and the Public Health Agency of Canada
Santé Canada et l'Agence de la Santé publique du Canada

# Evaluation of the Veterinary Drugs Program 1999 to 2012

Prepared by
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Health Canada and the Public Health Agency of Canada

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# List of Acronyms

| | |
|---|---|
| AAFC | Agriculture and Agri-Food Canada |
| ADE | Adverse Drug Experience |
| ADR | Adverse Drug Reaction |
| AFD | Animal Feed Division |
| *AMDUCA* | *Animal Medicinal Drug Use Clarification Act* |
| AMR | Antimicrobial resistance |
| AMRL | Administrative Maximum Residue Limit |
| ANDS | Abbreviated New Drug Submission |
| API | Active Pharmaceutical Ingredient |
| CAHI | Canadian Animal Health Institute |
| CAHPRAC | Canadian Animal Health Products Regulatory Advisory Committee |
| CBSA | Canadian Border Services Agency |
| CCRVDF | Codex Committee on Residues of Veterinary Drugs in Food |
| CCVB | The Canadian Centre for Veterinary Biologics |
| CED | Clinical Evaluation Division (VDD) |
| CFIA | Canadian Food Inspection Agency |
| CIELAP | Canadian Institute for Environmental Law and Policy |
| CIHR | Canadian Institutes of Health Research |
| CIPARS | Canadian Integrated Program for Antimicrobial Resistance Surveillance |
| CMIB | Compendium of Medicating Ingredient Brochures |
| CNISP | Canadian Nosocomial Infection Surveillance Program |
| COPD | chronic obstructive pulmonary disease |
| CVMA | Canadian Veterinary Medicine Association |
| DEL | Drug Establishment License |
| DFAIT | Department of Foreign Affairs and International Trade |
| DFO | Department of Fisheries and Oceans |
| DIN | Drug Identification Number |
| DPR | Departmental Performance Report |
| DSTS | Drug Submission Tracking System |
| EAC | Expert Advisory Committee |
| EAP | Expert Advisory Panel |
| EDR | Emergency Drug Release |
| EDRS | Emergency Drug Release Submission |
| ELDU | Extra-label drug use |
| EU | European Union |
| ESCS | Experimental Studies Certificate Submission |
| FCSAP | Food and Consumer Safety Action Plan |
| FDA | Food and Drug Administration |
| GMP | Good Manufacturing Practice |
| HPFB | Health Products and Food Branch (HC) |
| HRA | Health Risk Assessment |
| HSD | Human Safety Division (VDD) |
| IAS | Issue Analysis Summary |
| IFAH | International Federation for Animal Health |
| INDS | Investigational New Drug Submissions |
| LRHVP | Low-Risk Veterinary Health Products |
| MCED | Manufacturing and Chemical Evaluation Division (VDD) |
| MoRS | Management of Regulatory Submissions |

# List of Acronyms

| | |
|---|---|
| MOU | Memorandum of Understanding |
| MRL | Maximum Residue Limit |
| MRSA | methicillin-resistant *staphylococcus aureus* |
| MUMS | Minor Uses, Minor Species |
| NARMS | National Antimicrobial Resistance Monitoring System |
| NC | Notifiable Changes |
| NCRMP | National Chemical Residue Monitoring Program |
| NDS | New Drug Submission |
| NOC | Notice of Compliance |
| NOD | Notice of Deficiency |
| NON | Notice of Non-Compliance |
| OMCL | Official Medicines Control Laboratories |
| OTC | Over-The-Counter |
| OUI | Own-use importation |
| PAA | Program Activity Architecture |
| PHAC | Public Health Agency of Canada |
| PMF | Performance Measurement Framework |
| PMRA | Pest Management Regulatory Agency |
| PSUR | Periodic Summary Update Reports |
| RAPB | Regions and Programs Bureau |
| RCC | Regulatory Cooperation Council |
| RIA | Regulatory Impact Analysis |
| RIPP | Restricted Import Permit Program |
| RMAF | Results-based Management and Accountability Framework |
| SANDS | Supplemental Abbreviated New Drug Submission |
| SIMS | Stakeholder Information Management System |
| SIRC | Science Issues Review Committee |
| SNDS | Supplemental New Drug Submission |
| ToR | Terms of Reference |
| TPD | Therapeutic Products Directorate (HPFB) |
| TBS | Treasury Board of Canada Secretariat |
| VA | Veterinary antibiotics |
| VCPR | Veterinary-Client-Patient Relationship |
| VDD | Veterinary Drugs Directorate (HPFB) |
| VDP | Veterinary Drugs Program |
| VICH | International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products/ International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Products Program |
| WHO | World Health Organization |

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# Executive Summary

The Veterinary Drugs Program (VDP) is administered by the Veterinary Drugs Directorate (VDD) within the Health Products and Food Branch (HPFB) of Health Canada. The VDP is responsible for "evaluating and monitoring the safety, quality and efficacy of veterinary drugs administered to food-producing and companion animals, as well as promoting their prudent use and setting standards for such use" (Health Canada, 2010a). Program activities include conducting research and surveillance of health trends, developing policies and regulations, communicating with partners and stakeholders, conducting pre-market review and post-market surveillance of veterinary drugs, and monitoring/enforcing compliance with regulation. The program involves the following key program participants: the VDD; the HPFB Inspectorate, the Regions and Programs Bureau (RAPB) Regional Operations; and the Canadian Food Inspection Agency (CFIA).

The evaluation of the VDP is part of Health Canada's Five-Year Evaluation Plan. Using the current Treasury Board of Canada Secretariat *Policy on Evaluation* (TBS, 2009), the evaluation assessed the relevance and performance (effectiveness, efficiency, and economy) of Health Canada's activities under the VDP. The period of time that the evaluation covers is from 1999 to 2012. This time period was arrived at based on the *Health Products and Food Branch's Strategic Evaluation Plan* (2006) which identified the history of the Program's funding and concomitant reporting obligations. However, the main focus of the evaluation is on the later years of this time period. The results of the evaluation will inform the implementation of current and future activities of the VDP.

The data collection for the evaluation took place between February 2012 and August 2013 and drew on several lines of evidence, including a literature review, a document review, a review of administrative data, a comparative analysis of key issues, surveys of industry and veterinary drug end-users, and key informant interviews.

## Findings

### Relevance

The potential human health implications of veterinary drug use in food-producing and companion animals, such as those stemming from the potential presence of veterinary drug residues in food, the risks associated with development of antimicrobial resistance (AMR), and direct exposure to veterinary drugs, suggest an ongoing need for Health Canada to regulate these products in order to protect the health of Canadians. Such a role is consistent with federal and Health Canada roles and responsibilities, as described in federal statutes and regulations, and aligns directly with Health Canada's strategic outcome to inform and protect Canadians from health risks associated with food, products, substances, and environments. VDP activities are also well-aligned with federal priorities to strengthen food and consumer safety, as expressed in recent Speeches from the Throne, the Food and Consumer Safety Action Plan (FCSAP), and the Growing Forward Agreement. As part of HPFB's regulatory modernization initiative, the VDP is currently developing a new regulatory framework for veterinary drugs.

## Performance – program implementation

Regulatory authority for veterinary drugs in Canada is a shared jurisdiction of Health Canada, the CFIA, and the provinces and territories, with Health Canada and the CFIA responsible for carrying out pre- and post-market activities that are considered to be part of the VDP. Over the evaluation period, there has been no overall formal governance structure or coordinating mechanism for the VDP or the Health Canada component. However, Health Canada has a variety of formal and informal mechanisms and structures in place with its partners (e.g., Memoranda of Understanding, working groups and committees, etc.) to govern various aspects of the program. On the whole, the existing approach to program governance appears to be working reasonably well. Although there have been recent changes to HPFB's governance structure, under which veterinary drugs have been conceptualized as part of the larger Pharmaceutical Drugs Program, it remains important from both an accountability and a program management perspective that Health Canada retain its ability to report on both the outputs and the outcomes achieved of its regulatory activities related to veterinary drugs.

## Recommendation 1

**Health Canada should develop and strengthen its ability to report on the results of its regulatory activities related to the VDP.**

Health Canada has made considerable progress over the evaluation period in implementing its planned activities and, in the process, has responded to several emergent issues and challenges. One of its most notable accomplishments has been its success in eliminating a considerable backlog of veterinary drug submissions and dramatically reducing the average time to decision. The most recent available data indicate that in 2011–12, 89% of regulatory decisions for pharmaceutical veterinary drugs — compared to a performance target of 90% of decisions — were made within service standards. Health Canada has also undertaken several other initiatives to improve the efficiency of the review process, including launching a pilot project with the United States Food and Drug Administration (US FDA) on parallel review of the technical sections of companion animal submissions; introducing a voluntary Interim Notification Pilot Program for low-risk veterinary natural health products (LRVHPs); streamlining the review of generic drug submissions; introducing a specialized approval process for minor use, minor species (MUMS) drugs; and increasing information-sharing with international counterparts, including exploring ways to increase the use of foreign reviews and data.

With respect to communications and consultations with stakeholders, external key informants noted that the VDD has made a concerted effort, particularly in the last few years, to improve its communications to and consultations with stakeholders, and they generally believe that these communications and consultations have improved substantially. That being said, there is some evidence that while Health Canada has been particularly effective at communicating with industry, and somewhat effective at communicating with veterinarians, it has not been effective at reaching livestock producers. Given the implications of veterinary drug use for human health and food safety, it is important that livestock producers understand the risks associated with the

use of these products. A communication strategy could be implemented using intermediaries such as provincial veterinary associations and livestock producers to ensure Health Canada's risk communications are reaching veterinary drug end-users.

In the area of regulatory and policy development, although Health Canada has introduced a number of initiatives to address the complex problem of AMR, it has not yet fully implemented all of the 2002 recommendations of the Advisory Committee on Animal Uses of Antimicrobials and Impact on Resistance and Human Health. Its approach to date is also inconsistent with the 2011 recommendations of the World Health Organization (WHO), which include terminating non-therapeutic use of antimicrobials and requiring obligatory prescriptions for all antimicrobials used for disease control in food-producing animals. Health Canada key informants reported that the Department is currently proceeding with a number of initiatives to address AMR and is collaborating with the Public Health Agency of Canada (PHAC), the CFIA, Agriculture and Agri-food Canada (AAFC), and provincial/territorial authorities to develop a more coordinated approach to AMR.

Health Canada has been widely criticized by stakeholders for its failure to curtail the ongoing use of unapproved drugs, which is thought to be a major factor contributing to AMR. This practice is made possible by two features of the current regulatory framework for veterinary drugs. First, there is currently no prohibition against the import of unlicensed drugs for use on animals. This has enabled livestock producers to acquire less expensive veterinary products or products not available in Canada for use in their livestock operations. The other is current policies relating to active pharmaceutical ingredients (APIs), which are currently subject to minimal oversight by Health Canada. By comparison, other jurisdictions such as the EU and the US prohibit the importation and use of unlicensed veterinary drugs, and restrict the importation of bulk chemicals and APIs to holders of establishment licenses.

Recently, Health Canada has started the process to address the OUI and the importation and direct use of APIs by holding stakeholder consultations on a proposed regulatory approach to OUI and APIs in March 2013.

## Recommendation 2

**Health Canada should continue to take measures to address the importation and use of unlicensed veterinary drugs and APIs.**

Health Canada's pharmacovigilance activities for veterinary drugs include monitoring of adverse drug reaction reports, signal detection, causality assessment, and post-market actions such as label changes and drug recalls. Stakeholders who participated in this evaluation identified a number of potential shortcomings of Health Canada's approach to adverse drug reaction reporting and post-market surveillance, including under-reporting of adverse drug reactions by end-users; lack of awareness and understanding of Health Canada's adverse drug reaction reporting requirements among foreign manufacturers; lack of adverse drug reaction reporting requirements for unapproved imported products, including APIs; lack of attention to product efficacy in adverse drug reaction reports, which key informants said is important in the context

of AMR; and lack of post-market surveillance of veterinary natural health products (vNHPs). Moreover, unlike the US and the EU, information on the number and types of veterinary drug adverse reactions is not publicly reported in Canada.

Compliance and enforcement activities relating to veterinary drugs are carried out by Health Canada and the CFIA, and include education, consultation, and information; compliance monitoring through Good Manufacturing Practice (GMP) inspections and inspections for compliance with Maximum Residue Limits (MRL); compliance verifications and investigations; and the application of a variety of voluntary and/or regulatory compliance and enforcement measures in response to non-compliances. Health Canada's current approach to GMP inspections for veterinary drug establishments is perceived as problematic by the animal health products industry, which considers the Department to apply inappropriate guidelines stemming from a human health perspective to GMP inspections, including some that are not applied in the US or the EU. However, Health Canada has published specific guidance describing how GMP requirements may be applied differently in the case of veterinary drugs, and in recent consultations on a new regulatory framework for veterinary drugs, proposed that GMP requirements for veterinary drugs eligible under a proposed "registration" pathway would be introduced, similar to those prescribed in the *Natural Health Products Regulations.*

## Performance – achievement of outcomes

Over the evaluation period, Health Canada has engaged in many activities that should, in theory, contribute to the expected outcomes of the VDP. However, in most cases, administrative data to support conclusions on the extent to which outcomes have been achieved are limited. While the evaluation attempted to fill these gaps in information through the industry and end-user surveys, a small sample for the end-user survey resulted in limited reach and a low response rate. As a result of these factors, there are limited data on which to base definitive conclusions regarding achievement of outcomes.

In the immediate term, the VDP is expected to produce increased awareness and understanding by end-users of risks and benefits related to veterinary drugs, as well as increased awareness and understanding by industry of Health Canada's regulatory framework for veterinary drugs. While it seems clear that Health Canada has improved its communications and consultations with stakeholders in recent years, there is little evidence that these communications and consultations have produced the desired effect, particularly among end-users.

VDP activities are also intended to produce increased safety and effectiveness of veterinary drugs. The VDP contributes to product safety by establishing MRLs and administrative MRLs (AMRLs) for veterinary drugs, and had established 269 maximum residue limits for 88 pharmacologically active substances as of May 2012. Furthermore, recent improvements in the submission review process could, in theory, lead to more safe and effective drugs on the market. However, there is no evidence that new drugs are, in fact, safer and more efficacious than existing products.

In the immediate term, VDP activities are intended to produce increased industry compliance with Health Canada's regulatory framework for veterinary drugs. There is some evidence that industry compliance with established MRLs and GMP requirements is generally high, but due to a shift to combined reporting for veterinary and human drug GMP inspections in 2007–08, it is difficult to discern clear trends in GMP compliance within the veterinary drug industry. As the regulatory agency responsible for veterinary drugs, it is important for Health Canada to track and report on compliance within the veterinary drugs industry. Such an approach is arguably more consistent with the Department's recent move to recognize the uniqueness of veterinary drugs through a new regulatory framework for veterinary drugs, and would also be more consistent with the approach taken by the FDA, which separates compliance reporting by product line. A greater focus in reporting on compliance outcomes (rather than activities and outputs) would also contribute to greater understanding of industry compliance.

## Recommendation 3

**Health Canada should undertake to improve reporting on industry compliance with the regulatory requirements for veterinary drugs. Health Canada should also focus to a greater extent on compliance outcomes, as opposed to activities and outputs, in performance reporting.**

In the intermediate term, VDP activities are expected to lead external stakeholders to adopt safe behaviours associated with the use of veterinary drugs. There is some evidence from the literature that unsafe practices, including the use of antimicrobial agents, own-use importation, and importation and direct use of APIs, are taking place in Canadian agriculture, although the magnitude of the problem continues to be a matter of some debate. The impact of the VDP on end-user behaviour is an area for future research.

VDP activities are also expected to result, in the intermediate term, in increased use of scientific evidence and risk-benefit analysis by Health Canada to inform decision making. The use of scientific evidence and risk-benefit analysis is formally integrated into Health Canada's decision-making process, and, generally speaking, Health Canada appears to use scientific evidence and risk-benefit analysis on a regular basis to inform decision making. However, the Department has not yet implemented regulatory reforms to address importation and use of unapproved drugs. This appears to be, at least in part, due to concerns about the potential economic impact of such reforms for livestock producers.

In the intermediate term, VDP activities are expected to produce a timely response to identified risks. In the absence of performance standards or information on the amount of time Health Canada has taken to respond to specific identified risks, there is insufficient evidence to support general conclusions on this outcome. However, there are a few examples of long-standing issues that Health Canada has, so far, not addressed through policy and regulatory change — in particular, the ongoing practice of importation and use of unapproved veterinary drugs.

VDP activities are also expected to lead, in the intermediate term, to increased international harmonization of regulatory frameworks for veterinary drugs and, ultimately, to improved human health and safety of the food supply. The evaluation evidence suggests that Health

Canada has been active internationally. It participates in the International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products (VICH) and the Codex Alimentarius Commission, and has established several agreements on information-sharing and regulatory cooperation with international counterparts. While regulatory harmonization initiatives such as these may have the potential to contribute to improved human health and safety of the food supply, in the absence of any concrete evidence, the health and safety benefits of increased harmonization are more theoretical than real.

In the long term, VDP activities are expected to contribute to reduced health risks and adverse events associated with the use of veterinary drugs, increased safety of Canada's food supply, and increased public confidence in veterinary drugs, the related regulatory system, and the food supply. It seems reasonable to assume that VDP activities such as timely approval of safe and efficacious drugs, prohibitions on the sale of certain products for use in food-producing animals for which no residue level is considered safe, management of drug residues in food, initiatives to influence the use of antimicrobial agents in food-producing animals, and post-market surveillance and compliance activities should, in theory, contribute to the safety of the food supply and reduced health risks. Addressing the ongoing importation and use of unapproved veterinary drugs would further contribute to risk reduction and food safety.

As for public confidence in veterinary drugs, the related regulatory system, and the food supply, recent public opinion surveys suggest that, at present, Canadians are quite confident in Canada's food safety system; that they generally approve of Canadian standards and regulations in the area of food safety; and also that confidence in the Government of Canada may contribute significantly to their confidence in the food safety system itself. However, there are no public opinion data pertaining specifically to veterinary drugs.

## Performance – efficiency and economy

Changes in HPFB's approach to financial reporting over the evaluation period made it challenging to compare and analyze this information over time. Furthermore, HPFB recently has begun including veterinary drugs in financial reporting on the larger Pharmaceutical Drugs Program. HPFB has the ability to isolate the veterinary drugs-related activities of the VDD from its food safety-related activities for reporting. However, the VDP does not consist only of VDD activities, but also encompasses the activities of other program partners, such as the Inspectorate, RAPB, and RMOD. HPFB's current approach to financial reporting may not provide the total cost of the VDP. Furthermore, activity-based reporting, which is important to analysing program efficiency and economy, has not taken place since 2008-2009. From both a program management and an evaluation perspective, it is important to identify the total cost of the branch's veterinary drug-related activities and to analyze the cost drivers.

Due to significant weaknesses in the available financial and human resource information, the evaluation could not assess the extent to which program resources were used as planned, whether program outputs were produced efficiently, or whether expected outcomes were produced economically. That being said, there is evidence of improved operational efficiencies in recent years. The VDP has eliminated a considerable backlog of new drug submissions in recent years, drastically reduced the average time required to decide whether new drugs should be approved, and undertaken various other initiatives to improve the efficiency of pre-market review. Since many of these initiatives have been quite recent, their impact on program efficiency and economy has not yet been established. More extensive use of electronic submissions, acceptance of rolling submissions, acceptance of foreign data packages, and use of foreign reviews may introduce further efficiencies.

# Management Response and Action Plan

## Evaluation of the Veterinary Drugs Program[1]

| Recommendation (s) | Response | Key Activities | Deliverables | Responsible Directorate | Timeframe |
|---|---|---|---|---|---|
| 1. Health Canada should develop and strengthen its ability to report on the results of its regulatory activities related to the Veterinary Drugs Program (VDP). | Agree | Strengthen integrated business planning and reporting in HPFB at the program and subprogram levels as per the current PAA (2013-2014). | a) Assessment of current planning and reporting processes.<br>b) Implementation of a more rigorous process for integrated results-based reporting. | RMOD | a) Q4 2014-2015<br>b) Q1 2015-2016 |
| 2. Health Canada should continue to take measures to address the importation and use of unlicensed veterinary drugs and APIs. | Agree | HPFB will engage in consultations to explore options and international approaches to address the issue of "Own Use Importation" (OUI) and APIs in order to address concerns around food safety and public health.<br><br>As part of the proposed new Veterinary Drugs Regulatory Framework, the issue of OUI and APIs will be addressed at the regulatory level and will be supported by policy and program changes. | a) Consultations with stakeholders resulting in OUI and API policy and regulations.<br><br>b) Develop proposed policy instruments. | VDD | a) Q4 2013-2014<br>b) Q4 2014-2015 |

[1] This MRAP has been developed by participating organizations [i.e., Veterinary Drugs Directorate (VDD), Resource Management and Operations Directorate (RMOD), and the HPFB Inspectorate (Inspectorate), of the HPFB); and the Regions and Programs Bureau (RAPB)] in response to the recommendations made in the Evaluation of the Veterinary Drugs Program. *All responsibility for reporting on key activities rests at the Director General level.*

| Recommendation (s) | Response | Key Activities | Deliverables | Responsible Directorate | Timeframe |
|---|---|---|---|---|---|
| 3. Health Canada should undertake to improve reporting on industry compliance with the regulatory requirements for veterinary drugs. Health Canada should also focus to a greater extent on compliance outcomes, as opposed to activities and outputs, in performance reporting. | Agree | Health Canada currently uses the overall compliance rating (i.e. % compliance) of industry as an outcome based performance indicator to measure and assess the results of the Inspectorate's outputs (i.e. inspection targets, # of incidents opened/closed) in achieving program objectives. This performance measure is reported monthly and included in the Health C Dashboard, as well as used in the Departmental Performance Report, Report on Plans and Priorities, and Performance Measurement Framework (PMF).<br>Since the period reviewed in this evaluation, Health Canada has also developed an Annual Inspection summary report for external publication. The report describes in detail the overall compliance rate of industry per program and lists the common observations cited in non-compliant establishments. It also provides specific examples of observations cited against the *Food and Drugs Act* and *Regulations* and provides links between inspections conducted by activity (i.e. manufacturer, importer, distributor, etc.), observations noted and their associated risk category. The aim of publishing this report is to address many of the performance outcomes in the PMF, including "Increased awareness and understanding among industry of Health Canada's regulatory framework", and "Increased industry compliance with Health Canada's regulatory requirements." | First annual inspection summary report prepared for publication. | Inspectorate | March 2014 |

# 1. Introduction

The Veterinary Drugs Program (VDP) is administered by the Veterinary Drugs Directorate (VDD) within the Health Products and Food Branch (HPFB) of Health Canada. The VDP is responsible for "evaluating and monitoring the safety, quality and efficacy of veterinary drugs administered to food-producing and companion animals, as well as promoting their prudent use and setting standards for such use" (Health Canada, 2010a). Program activities include conducting research and surveillance of health trends, developing policies and regulations, communicating with partners and stakeholders, conducting pre-market review and post-market surveillance of veterinary drugs, and monitoring/enforcing compliance with regulation. The program involves the following key program participants: the VDD; the HPFB Inspectorate, Regional and Programs Bureau (RAPB) Regional Operations; and the Canadian Food Inspection Agency (CFIA).

The evaluation of the VDP is part of Health Canada's Five-Year Evaluation Plan. Using the current Treasury Board Policy on Evaluation (TBS, 2009), the evaluation assessed the relevance and performance (effectiveness, efficiency, and economy) of Health Canada's activities under the VDP, covering the period from 1999 to 2012.[2] This time period was arrived at based on the Health Products and Food Branch's Strategic Evaluation Plan (2006) which identified the history of the Program's funding and concomitant reporting obligations. However, the main focus of the evaluation is on the later years of this time period. The results of the evaluation will inform the implementation of current and future activities of the VDP.

Prairie Research Associates Inc., an independent evaluation consulting firm, conducted the evaluation on behalf of Health Canada. The data collection for the evaluation took place between February 2012 and August 2013 and drew on several lines of evidence, including a literature review, a document review, a review of administrative data, a comparative analysis of key issues, surveys of industry and veterinary drug end-users, and key informant interviews. This report presents the evaluation findings, draws conclusions, and makes recommendations.

## 1.1 Organization of the report

The report is organized in several sections. Section 2 describes a detailed program profile for the VDP, Section 3 describes the methodology, and Section 4 provides the evaluation findings. Section 5 concludes and makes recommendations. Three appendices accompany the main report. Appendix A contains the evaluation matrix, Appendix B contains the list of references, and Appendix C contains supplementary data tables.

[2] Although the CFIA is a partner in the VDP, its activities are not subject to this evaluation. However, these activities are described for contextual purposes.

# 2. Profile of the VDP

The VDP is responsible for "evaluating and monitoring the safety, quality and efficacy of veterinary drugs administered to food-producing and companion animals, as well as promoting their prudent use and setting standards for such use" (Health Canada, 2010a). This section describes the roles and responsibilities of VDP partners, the activities of the program, and expected outcomes.

## 2.1 Roles and responsibilities of VDP partners

The VDP involves four key program participants: the VDD, the Inspectorate, RAPB Regional Operations, and the CFIA.

### 2.1.1 VDD

The VDD, established in October 2001, is the main entity responsible for evaluating and monitoring the safety, quality and efficacy of veterinary drugs, and for promoting their prudent use and setting standards for their use. The VDD consists of five divisions and a Director General's Office, which is responsible for planning and administration and for the financial operation of the VDD (Health Canada, 2010b). The roles and responsibilities of the VDD's five divisions are summarized below.

**Human Safety Division (HSD)**

- Determines whether veterinary drugs pose a risk to human health through the following:
    - assessment of the pharmacology/toxicology of the drug to derive the acceptable daily intake and determine if it is a toxin/carcinogen for humans.
    - (for microbial drugs) assessment of the microbiological safety of the drug to calculate the microbiological acceptable daily intake of the drug if it is ingested by humans through food sources and to assess the impact of the use of the drug in animals on human medicine.
    - calculation of the maximum residue limit of the drug product and associated withdrawal period (if applicable).
- Provides national standards regarding residues of veterinary drugs that can remain in foods of animal origin (e.g., establishing maximum residue limits).
- Performs Health Risk Assessments (HRAs) and related recommendations (conducted upon request for drug residue violations found during inspections where there are no established maximum residue levels or tolerances).
- Develops policies and regulations relating to human safety of veterinary drugs
- Promotes prudent use of veterinary drugs, specifically as it relates to antimicrobial drugs and its impact on antimicrobial resistance.

**Manufacturing and Chemical Evaluation Division (MCED)**

- Performs pre-market assessments of complete production processes of veterinary drugs to ascertain if they meet acceptable quality standards.
- Monitors production processes related to veterinary drugs to ensure that they meet acceptable quality and manufacturing standards.
- Performs HRAs and provides related recommendations in circumstances where the quality aspects of a veterinary drug may impact human or animal safety.
- Completes assessment of post-market changes to the production processes of veterinary drugs.
- Develops policies and guidance documents related to the quality of veterinary drugs.

**Clinical Evaluation Division (CED)**

- Performs pre-market evaluations of veterinary drugs to ascertain safety and effectiveness.
- Monitors veterinary drug labels for clarity, concision, and adequate directions for us.
- Monitors veterinary drugs that are in the market through post-market surveillance activities (also referred to as pharmacovigilance).
- Promotes prudent use of veterinary drugs that are in the market.
- Oversees the Emergency Drug Release (EDR) program, which permits manufacturers to sell small quantities of new drugs not approved in Canada to veterinary practitioners in special circumstances.
- In conjunction with HSD and MCED, evaluates proposals for clinical trials.

**Submission and Knowledge Management Division (SKMD)**

- Manages veterinary drug submissions and develops related policies.
- Verifies that submissions are veterinary drugs and fall within VDD's mandate.
- Screens submissions for completeness and quality; requests clarification from sponsors as needed.
- Distributes submissions to relevant divisions for review and compiles their respective recommendations.
- Forms a VDD position on the veterinary drug product and informs the sponsor of the decision.
- Engages in reconsideration process with sponsor (if warranted).

**Policy, Regulatory and International Affairs Division (PRIAD)**

- Develops policies, guidelines, and regulations to address issues relating to the review of drug submissions for veterinary drugs or the protection of Canada's food supply and human and animal health.

- Plans and coordinates international activities for VDD, including bilateral activities with other regulatory agencies and participation in the Codex Alimentarius Commission (Codex) and the International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products (VICH).
- Promotes and maintains stakeholder involvement in VDD's activities.

### 2.1.2 Inspectorate and RAPB

The Inspectorate and the RAPB Regional Operations are responsible for delivering the Inspectorate Program. The Inspectorate's main role is "to deliver a national compliance and enforcement program for all products under the mandate of the Branch, with the exception of food products [along with medicated feeds and veterinary biologics] that are the responsibility of the Canadian Food Inspection Agency" (Health Canada, 2011a). With respect to veterinary drugs, the Inspectorate's responsibilities include the following:

- licensing veterinary drug establishments and conducting inspections to ensure compliance with Good Manufacturing Practices (GMP).
- conducting compliance verifications and investigations when a potential non-compliance is identified or brought to the attention of the Inspectorate.
- encouraging or enforcing compliance by regulatees through the use of a variety of voluntary and/or regulatory approaches; while compliance is normally achieved through cooperation between the Inspectorate and the regulatee, the Inspectorate can turn to non-voluntary enforcement options if required (Inspectorate, 2005a).
- administering recalls, which are defined as "a firm's removal from further sale or use, or correction, of a distributed product that presents a risk to the health of consumers or violates legislation administered by the [HPFB]" (Inspectorate, 2005a); recalls typically are conducted voluntarily by the regulated party.
- providing chemical, physical, and microbiological analysis services through the Laboratory Program to support inspection and investigation activities.
- examining personal and commercial veterinary drug shipments at the border for compliance with Canadian regulations.
- requesting that the VDD conduct HRAs in response to potential health risks identified through the course of compliance activities.
- recommending that Health Canada inform the public of imminent risks to health by means of a public warning or public advisory.
- conducting compliance promotion activities with industry stakeholders.

In response to non-compliance, the Inspectorate takes a risk-based approach in working with the regulated party to ensure appropriate actions, such as product stop sales, recalls, and/or public communications, have been taken. The Inspectorate also may undertake enforcement actions such as product seizures, import alerts, or criminal investigations, when needed.

RAPB is the operational arm of Health Canada in the regions and provides services to Canadians in every province and territory. Responsibilities include compliance promotion activities, as well as enforcement of laws and regulations through inspections, investigations, legal action, and evaluations of compliance with standards affecting manufacturing, packaging and labelling, analysis, importing, distributing, and wholesaling of consumer health products, including veterinary drugs.

### 2.1.3 CFIA

While the evaluation of the VDP is not evaluating the CFIA's activities per se, the CFIA, like Health Canada, plays an important role in regulating veterinary drugs.

The CFIA's responsibilities include monitoring of adherence to maximum residue limits (MRLs) of chemicals in food products, including chemicals related to veterinary drugs. These MRLs are set by the VDD under the authority of the *Food and Drugs Act and Regulations* (CFIA, 2012). New veterinary drugs approved by the VDD are subject to CFIA monitoring, and the Agency has the ability to provide enforcement in the event of a violation. The VDD plays an advisory role to the CFIA in the event of violations, providing the Agency with risk assessments (Health Canada, 2011b).

The CFIA also is responsible for regulating veterinary biologics, as laid out in the *Health of Animals Act and Regulations*. In this regard, the Agency's roles and responsibilities include issuing licences to manufacturers of veterinary biologics, issuing licences for veterinary biologics products, issuing import permits, establishing withdrawal times, approving label claims for different disease conditions, issuing export certificates, collaborating with the Canadian Border Services Agency (CBSA) for border inspections, and conducting pharmacovigilance. The Canadian Centre for Veterinary Biologics (CCVB) is responsible for regulating the manufacturing and importation of veterinary biologics.

Finally, the CFIA regulates feeds under the authority of the *Feeds Act*. In collaboration with the VDD, the CFIA's Animal Feed Division (AFD) maintains the Compendium of Medicating Ingredients Brochures (CMIB), which lists the brands of medicating ingredients that have been approved by Health Canada for over-the-counter use in medicated livestock feeds. The CFIA is also responsible for verifying that veterinary drugs are being used in livestock feeds as approved and that non-medicated feeds do not contain unsafe drug residues. Where products pose unacceptable risk to animal health or production, or may result in human health risk due to residues in foods, product recalls and other product control actions are implemented.

Because of overlap in the definitions for a "drug" in the *Food and Drugs Act* and a "feed" in the *Feeds Act*, the VDD and the CFIA currently collaborate to determine the regulatory status of individual products. The AFD within the CFIA is responsible for these activities.

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## 2.2 Logic Model

**Table 1: Logic Model for the Veterinary Drugs Program**

| Inputs | Funding | Human Resources | Facilities, infrastructure | Acts, Regulations, policies | Science and technology | Research data |
|---|---|---|---|---|---|---|
| **Activities (A)** | (1) Provide and conduct research and surveillance | (2) Develop science-based policies and regulations | (3) Communicate and engage partners and stakeholders | (4) Conduct pre-market activities and standard setting | (5) Conduct post-market surveillance and monitoring activities | (6) Provide advice/support and conduct enforcement activities |
| **Outputs (B)** | • Reports<br>• Methodologies (improved residue detection)<br>• Data (e.g., residues/antimicrobial resistance trends) | • Policies, regulations, guidelines, guidance documents<br>• Memoranda of Understanding for national/international cooperation agreements | • Stakeholder educational materials/events/meetings<br>• Consultations<br>• Notifications (e.g., public advisories and health professional communications), responses to inquiries, correspondence | • Administrative maximum residue limits/maximum residue limits<br>• Risks assessments<br>• Standards<br>• Authorizations<br>• Risk management plans | • Up-to-date labeling<br>• Periodic summary update assessments<br>• Risk assessments<br>• Risk management plans<br>• Risk management decisions<br>• Adverse Drug Reaction (ADR) reports | • Health Risk Assessments, Health Hazard Evaluations<br>• Drug status decisions<br>• Reports and regulatory recommendations<br>• Establishment licenses<br>• Mutual recognition agreements<br>• Compliance and verification reports<br>• Inspection reports<br>• Laboratory analyses<br>• Recalls |
| **Target Groups (C)** | • Federal regulators (CFIA, PHAC)<br>• International stakeholders | • Industry<br>• Federal/provincial/territorial and international regulatory stakeholders/partners<br>• End users<br>• Advisor committees<br>• Professional associations<br>• Academia | • Federal regulators<br>• Sponsors/applicants<br>• International regulators<br>• Industry<br>• Professional associations<br>• End users | • International and federal regulators<br>• Sponsors/applicants<br>• Market authorization holders<br>• End users<br>• Professional associates<br>• Academia | • Federal/provincial/territorial and international regulatory stakeholders/partners<br>• Industry<br>• Public/end users<br>• Sponsors/applicants | |
| **Immediate Outcomes (D)** | Increased awareness and understanding among external stakeholders of risks and benefits related to veterinary drugs | Increased awareness and understanding among industry of Health Canada's regulatory framework for veterinary drugs | Increased safety and effectiveness of veterinary drugs | Increased industry compliance with Health Canada's regulatory requirements related to veterinary drugs | | |
| **Intermediate Outcomes (E)** | Adoption of safe behaviours associated with veterinary drugs by external stakeholders | Increased use of scientific evidence and risk-benefit analysis by Health Canada to inform decision making | Timely regulatory system response to identified risks | International harmonization of regulatory frameworks for veterinary drugs, contributing to improved health of Canadians and increased safety of Canada's food supply | | |
| **Long-Term (F)** | Reduced health risks and adverse events associated with the use of veterinary drugs | The VDP contributes to the safety of Canada's food supply | Increased public confidence in veterinary drugs, the regulatory system, and the food supply | A sustainable, cost-efficient, responsive, and science-based regulatory system for veterinary drugs in Canada | | |
| **Ultimate Outcome** | Improved health and well-being of Canadians | | | | | |

## Description of the Logic Model (Table 1)

The VDP consists of six main activities delivered by Health Canada and the CFIA, although, as already noted, evaluation coverage is focussed on Health Canada's activities.

Provide support and conduct research and surveillance. The VDD sponsors and supports research and surveillance with internal and external partners. These activities are intended to enhance sound policy and regulatory development, ultimately improving human and animal health and the safety of the food supply. These activities include, for example, research into drug residue detection methodologies; residue monitoring; and surveillance of antimicrobial resistance. These activities are expected to lead to the following outputs: reports, methodologies (e.g., improved residue detection) and data (e.g., residues/antimicrobrial resistance trends). The target groups for these activities are: federal regulators (i.e., CFIA and PHAC) and international stakeholders.

Develop science-based policies and regulations. This activity involves the development and implementation of various types of legislation, regulations, policies, guidance documents, and Memoranda of Understanding (MOU) related to maintaining and improving the regulatory framework for veterinary drugs. These activities are expected to lead to the following outputs: policies, regulations, and guidance documents and memorandum of understanding for national/international cooperation agreements. The target groups for these activities are: industry, federal/provincial/territorial and international regulatory stakeholders and partners, end users, advisor committees, professional associations and academia.

Communicate and engage partners and stakeholders. Through this activity, the VDP communicates via a variety of mechanisms with partners and stakeholders, including the general public, industry, health professionals, academics and researchers, and others. This activity also includes consultations with stakeholders on issues related to veterinary drugs (e.g., consultations with industry on draft guidance documents). These activities are expected to lead to the following outputs: stakeholder educational materials, events, meetings, consultations, notifications (e.g., public advisories and health professional communications), responses to inquiries and correspondence. The target groups for these activities are: industry, federal/provincial/territorial and international regulatory stakeholders and partners, end users, advisor committees, professional associations and academia.

Conduct pre-market activities and standard-setting. This activity consists of pre-market review of veterinary drug submissions from industry to determine if these products are safe and effective and to determine if labelling is clear and concise. Drugs used in food-producing animals are, in addition, assessed for their potential risks to human health. This activity also includes the establishment of withdrawal periods and MRLs. These activities are expected to lead to the following outputs: administrative maximum residue limits/maximum residue limits, risk assessments, standards, authorizations and risk management plans. The target groups for these activities are: federal regulators, sponsors/applicants, international regulators, industry, professional associations and end users.

Conduct post-market surveillance and monitoring activities. Through this activity, the VDP monitors the safety, efficacy, and quality of veterinary drugs on the market by collecting and

analysing information on reported issues, concerns, or adverse drug reaction reports, and requesting Periodic Summary Update Reports (PSURs). This activity also includes conducting different types of residue and contamination monitoring. The monitoring data are analysed and used to develop and publish information on veterinary drug hazards and to recommend corrective actions. This activity also includes collaborating with the Public Health Agency of Canada (PHAC) in monitoring antimicrobial resistance trends through the Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS). These activities are expected to lead to the following outputs: up-to-date labeling, periodic summary update assessments, risk assessments, risk management plans, risk management decisions and adverse drug reaction reports. The target groups for these activities are: international and federal regulators, sponsors/applicants, market authorization holders, end users, professional associates and academia.

Provide advice/support and conduct compliance and enforcement activities. These activities are aimed at monitoring and enforcing compliance with the *Food and Drugs Act* and Regulations through a number of activities, such as compliance verifications, inspections, establishment licensing, border integrity, and supporting laboratory activities. In the event of non-compliance, a variety of enforcement options may be implemented, including the stop sale or recall of a product; product seizures; searches; and prosecution. Finally, this activity includes surveillance and monitoring of residues of veterinary drugs in domestic and imported foods, which is carried out by the CFIA. These activities are expected to lead to the following outputs: health risk assessments, health hazard assessments, drug status decisions, reports and regulatory recommendations, establishment licenses, mutual recognition agreements, compliance and verification reports, inspection reports, laboratory analyses and recalls. The target groups for these activities are: federal/provincial/territorial and international regulatory stakeholder/partners, industry, public/end users and sponsors/applicants.

Together these activities and outputs are expected to lead to the following outcomes:

In the immediate term, VDP activities are expected to lead to increased awareness and understanding among external stakeholders of risks and benefits related to veterinary drugs and increased awareness and understanding among industry of Health Canada's regulatory framework for veterinary drugs, as well as increased safety and effectiveness of veterinary drugs and increased industry compliance with the regulatory framework.

The achievement of these immediate outcomes is expected to lead to several intermediate outcomes: adoption of safe behaviours associated with veterinary drugs by external stakeholders; increased use of scientific evidence and risk-benefit analysis by Health Canada to inform decision making; and timely regulatory response to identified risks. Additionally, international harmonization of regulatory frameworks for veterinary drugs is expected to contribute to improved health of Canadians and increased safety of Canada's food supply.

In the long term, Health Canada hopes to reduce health risks and adverse events associated with the use of veterinary drugs; increase public confidence in veterinary drugs, the related regulatory system, and the food supply; contribute to the safety of the food supply; and produce a sustainable, cost-efficient, responsive, and science-based regulatory system for veterinary drugs in Canada.

These outcomes are expected to contribute to Health Canada's ultimate goal of improving the health and well-being of Canadians.

# 3. Methodology

This section of the report provides a detailed description of the evaluation methodology. The section includes a list of the evaluation issues and questions; a description of the evaluation design, data collection methods, and approach to data analysis; and a discussion of the limitations of the methodology, as well as mitigation strategies.

## 3.1 Evaluation questions

The evaluation addresses 10 key questions and a number of sub-questions. Appendix A contains a detailed evaluation matrix that links each question to a set of indicators, data sources, and collection methods. The evaluation questions and the matrix conform to the Treasury Board of Canada's Policy on Evaluation.

## 3.2 Evaluation design and data collection methods

The evaluation design was developed based on the findings of an evaluability assessment, completed as a first step in the evaluation. The evaluability assessment consisted of a preliminary review and assessment of available documents and administrative data, as well as 14 preliminary interviews with key program stakeholders, including representatives of the VDD, the Inspectorate, and the CFIA. The evaluation design and the evaluation matrix (Appendix A) were developed based on the evaluability assessment.

The evaluation consisted of several data collection methods.

Literature review. The literature review addressed evaluation questions related to program relevance, long-term outcomes, and alternate approaches. Peer-reviewed (i.e., scientific and academic), as well as grey, literature was considered in the review. Relevant literature was located through online searches.

Document review. The document review addressed all the evaluation questions, to the extent that supporting documents were available. The review encompassed government documents, primarily produced by Health Canada and the CFIA, related to VDP planning, management, and ongoing operations. Several hundred documents were reviewed as part of the evaluation.

Administrative data review. The administrative data review addressed evaluation questions related to program outcomes. The review considered data produced by the VDD, the Inspectorate, and the CFIA. Although theoretically distinct, the document review and the administrative data review were, in practice, two aspects of the same task, as the majority of administrative data was included in program documents.

Comparative analysis of key issues in veterinary drug regulation. The key issues analysis expanded the literature and document review, with the goal of examining a number of key topics in veterinary drug regulation that came to light through the literature and document review task. The objectives of the key issues analysis was to describe Canada's response to the issues identified, to consider how domestic and international stakeholders have viewed this response, and to describe how other jurisdictions, namely the United States (US) and the European Union (EU) have approached the same issues.

Survey of industry. The bilingual survey of industry used a web-based approach and focussed on evaluation questions related to outcomes. The survey targeted manufacturers of veterinary drugs, as well as industry consultants. Potential survey sample was provided by the Canadian Animal Health Institute (CAHI), the main industry association for veterinary drugs in Canada. A total of 30 names were identified by CAHI. Duplicate or multiple contacts from the same organization were removed, as were individuals who had already participated in a key informant interview. After cleaning, the final sample consisted of 20 industry representatives, each from a different organization. The survey achieved 10 completions, representing a completion rate of 50%.

Survey of veterinary drug end-users. The bilingual end-user survey used a web-based methodology and targeted veterinarians, animal health technologists, and representatives of livestock producer associations, some of whom may also be livestock producers themselves. The sample was compiled from a list provided by Health Canada, consisting of VDD stakeholders within Health Canada's Stakeholder Information Management System (SIMS) database; this list consisted primarily of representatives of producer associations. A small number of additional names, primarily veterinarians, were identified by the VDP in response to a request by the evaluators. The final sample of 275 consisted of 215 representatives of livestock producer associations and 60 veterinarians and animal health technologists. The survey achieved a response rate of 12% (32 out of 267 valid addresses) and a completion rate of 8% (21 out of 267 valid addresses).

External key informant interviews. The key informant interviews addressed all of the evaluation questions. A total of 36 external key informants were interviewed. These included representatives of parts of Health Canada not involved in VDP delivery and of other federal departments (n=10); provincial veterinary medical associations and other provincial regulatory bodies (n=11); livestock producer associations (n=4); academics and researchers (n=4); industry (n=3); consumer associations (n=1); and other external stakeholders (n=3). Key informants were identified by the evaluators using purposive sampling — that is, key informants were selected for their specific knowledge, expertise, and/or involvement with the VDP, and for the unique insights that they would each bring to the evaluation.

All key informants received an email invitation from Health Canada to participate in the evaluation and received a copy of the interview guide in advance so that they could provide considered responses. Interviews were conducted in key informants' preferred official language and were digitally recorded with the permission of key informants. Key informants were given the opportunity to review and edit the notes to ensure accuracy, and were assured of the confidentiality of their responses.

Internal key informant interviews. In addition to the preliminary interviews with 14 representatives of the VDP completed at the project outset, a second round of interviews with nine Health Canada representatives was completed following completion of the other data collection activities. This round of interviews was intended to allow program personnel the opportunity to respond to some of the preliminary evaluation findings, and to provide additional information, including additional documents and data, as necessary. As with the external interviews, internal interviews were recorded (with permission) and notes were returned to interviewees for review.

## 3.3 Approach to data analysis

Three technical reports were produced through the course of the study, summarizing the findings from the literature review, the document review, and the administrative data review; the key issues analysis; and the surveys and external interviews. Program personnel reviewed and commented on the first two technical reports and reviewed the third technical report. In addition, during the second round of interviews, internal Health Canada interviewees were given an opportunity to respond to the preliminary findings, providing alternate interpretations and/or additional data. This process added nuance to the interpretation of the data and helped to validate the evaluation findings.

The document, data and literature review report, the key issues analysis, and the final report were also reviewed by a scientific expert in veterinary pharmacology who was contracted to participate on the research team. The input of the expert was essential to ensuring that relevant scientific information was presented in an accurate and balanced way.

For final reporting, data from all lines of evidence was integrated or triangulated in order to arrive at the overall evaluation findings. Triangulation is a process through which answers to research questions generated by different data collection methods are compared. Where different methods produced similar findings, those findings were assumed to have greater validity and therefore greater confidence in the results is warranted.

## 3.4 Limitations of the methodology and mitigation strategies

There are several important methodological limitations to note, associated primarily with the surveys. Although the surveys were intended to address the data gaps noted above, the way in which the survey samples had to be derived limited the extent to which they could achieve this purpose. More specifically, guidance and direction from the Treasury Board of Canada Secretariat on public opinion research and surveys limited the evaluators to surveying contacts who were known to have had contact with the Department for reasons related to the VDP. In the case of the industry survey, the sample of industry contacts was provided by CAHI and is presumed to include most, if not all, Canadian-based manufacturers of veterinary drugs. While the industry survey achieved a good response rate (50%), it did not include manufacturers based outside of Canada, who are subject to Canadian regulations in order to market their products in this country.

For the end-user survey, the evaluation had to rely on stakeholder lists maintained by Health Canada, rather than using other, potentially more complete, external sources. This approach to sample development had two important consequences.

- The end-user survey was dominated by representatives of livestock producer associations, who had the highest number of stakeholders within Health Canada's internal stakeholder lists. It is unknown how many of these representatives were livestock producers (i.e., end-users) themselves. It is possible that those who were not producers may have felt that the survey did not apply to them, and thus did not participate in the survey. This may, in part, explain the low response rate achieved by this survey. In any event, the end-user survey reached only a tiny fraction of all livestock producers in Canada.
- The reliance on Health Canada's stakeholder lists also meant that the sample had relatively minimal representation from veterinarians. The sample included 60 veterinarians and animal health technologists, compared with a potential sample of several thousand.[3] This is a very significant shortcoming, considering that veterinarians are one of the VDP's most important end-user groups.

While some results from the industry and end-user surveys are included in this report, it is important to remember that the results are not statistically significant and do not represent the views of all veterinary drug manufacturers or end-users. To mitigate the limitations of the surveys, the evaluation relied heavily on more objective evidence from the literature review, the document review, and the administrative data review.

Though not a methodological limitation per se, it is also important to acknowledge the specific role of the qualitative key informant interviews in the evaluation. As noted above, external key informants were selected for their specific knowledge, expertise, and/or involvement with the

[3] For example, over 7,200 veterinarians are members of the Canadian Veterinary Medical Association (CVMA) (CVMA, 2011). The CVMA does not include all veterinarians in Canada, since some provincial veterinary medical associations do not require CVMA membership.

VDP, and for the unique insights that they would each bring to the evaluation. As a result of their specialized areas of expertise and experience, most key informants were not able to address all of the interview questions, but rather focused on topics about which they were most knowledgeable. As such, the role of the key informant interviews within the evaluation was not to quantify how widely held various opinions are within the VDP's stakeholder population (that was the objective of the surveys). Rather, it was to identify salient issues and concerns raised by key program stakeholders. In a context where key informants are chosen for their specific knowledge and expertise, it is important to recognize that to be valid, points of view need not be shared by all key informants.

Finally, although some information on financial and human resources was provided to the evaluation, the extent to which program efficiency and economy could be analyzed was limited by the available data.

# 4. Findings

This section of the report presents the evaluation findings, organized by evaluation issue.

## 4.1 Relevance

### 4.1.1 Ongoing need for the VDP

**The potential human health implications of veterinary drug use in food-producing and companion animals suggest a continued need for regulatory intervention in this area in order to protect the health and safety of Canadians.**

A wide range of health products is currently employed in veterinary medicine, including, but not limited to, antimicrobial agents, analgesics, anti-inflammatory agents, anaesthetics, anti-parasitic agents, vaccines, and natural health products. The potential human health implications of veterinary drug use in food-producing and companion animals suggest a continued need for regulatory intervention in this area.

**Veterinary drug residues in food**

A key route of human exposure to veterinary drug residues is through the food supply, primarily through consumption of animal tissues or by-products containing residues. The scientific literature suggests these residues may pose a variety of human health risks, although it is also important to note that in some cases, considerable scientific uncertainty remains regarding impacts on human health.

Many studies suggest that residual antimicrobials can contribute to resistant bacteria in the gastrointestinal tract, causing disruption in the microfloral intestinal barrier and leaving the intestinal tract less able to digest nutrients and more vulnerable to disease (Doyle, 2006, p. 2;

Tollefson & Miller, 2000, p. 249). The VICH (2004) found no reports of human health effects resulting from changes in the proportion of AMR bacteria in human intestinal flora, but notes that, given the limitations of current understanding of microbial ecology, the potential for adverse health effects should not be dismissed.

While rare, allergic or anaphylactic reactions to veterinary drug residues are also possible. For instance, Raison-Peyron, Messaad, Bousquet, and Demoly (2001) note 20 cases involving anaphylaxis and suspected penicillin residues in beef and pork. These reactions tend to occur among individuals with pre-existing sensitivities to these drugs. Doyle (2006) notes that, while uncommon, there have been reports of veterinary drug residues in meat causing allergic reactions in humans. VICH (2002) guidance document GL33 recommends investigating certain drug classes, such as beta-lactam antibiotics, because these drugs can cause allergic reactions in sensitive individuals.

Other types of human health effects may also result from exposure to veterinary drug residues. For example, Barbosa et al. (2005) refer to four separate Portuguese cases of acute food poisoning (involving 50 individuals) resulting from ingestion of meat and liver containing clenbuterol residue. The authors also cite studies in other jurisdictions connecting cases of food poisoning to ingestion of liver and meat containing clenbuterol residues. As another example, the antimicrobial agent chloramphenicol can cause aplastic anemia (bone marrow suppression) in human beings (Turnipseed & Andersen, 2008, p. 316).

There is also evidence that in the longer term, the presence of drug residues in food may have carcinogenic or reproductive/teratogenic effects. For example, scientific evidence suggests that Leuco-malachite green may be a genotoxic carcinogen; consequently, its deliberate use in food-producing animals is not permitted in Canada (CFIA, 2006a). As another example, furazolidone and its metabolites are known to induce cancer in animals, while diethylstilbestrol can have reproductive/teratogenic effects. Indeed, due to their adverse effects on human health, the sale of several substances for use in food-producing animals is prohibited under the *Food and Drug Regulations*, including chloramphenicol or its salts or derivatives; 5-nitrofuran compounds; clenbuterol or its salts or derivatives; 5-nitroimidazole compounds; or diethylstilbestrol or other stilbene compounds (GoC, 2012a, sec. c.01.610.1).

Results from national residue monitoring programs in Canada, the US, and the EU suggest that while foods sometimes test positive for drug residues, it is rare for these residues to exceed established tolerance levels (CFIA, 2008a, 2011a; European Food Safety Authority, 2010; US Department of Agriculture, 2011, pp. 40, 65–66).

### Antimicrobial resistance (AMR)

Use of antimicrobial agents in medicine has enabled treatment of diseases which previously represented significant contributors to morbidity and mortality in human beings. However, AMR is widely considered a serious threat to public health because it erodes the efficacy of these agents in treating a wide range of diseases in human beings. Numerous studies have shown that AMR infections contribute to increased hospitalization rates, greater disease severity, increased health care costs, and higher mortality; for a summary of the findings from some of these studies, please see Appendix C.

Antimicrobial agents are used in Canadian livestock production in the treatment and prevention of disease, as well as in growth promotion (Rosengren, Gow, & Weese, 2009, pp. 25–27; Sarmah, Meyer, & Boxall, 2006). However, the use of antimicrobial agents for growth promotion and prophylaxis (i.e., disease prevention) in animals is currently controversial.[4] The Canadian Institute for Environmental Law and Policy (CIELAP) recently recommended that Canada ban or restrict the use of antibiotics for these purposes (Holtz, 2009, p. 6). Likewise, a comprehensive review of the literature on the relationship between industrial food animal production and antimicrobial resistance concluded that "the use of antimicrobials for nontherapeutic purposes in agriculture is a major factor driving the emergence of antimicrobial resistance globally," and argued that "prudent public health policy thus indicates that nontherapeutic uses of antimicrobials in food animal production should stop" (Silbergeld, Graham, & Price, 2008, p. 162). For similar reasons, in its 2011 policy package for combating AMR, the WHO recommends terminating nontherapeutic use of antimicrobials — such as the use of antimicrobials as growth promoters — as well as restricting or eliminating the use in food-producing animals of antimicrobials that are seen as critically important in human medicine (especially fluoroquinolones and third- and fourth-generation cephalosporins); and requiring obligatory prescriptions for all antimicrobials used for disease control in food-producing animals (WHO, 2011).

On the other hand, it is important to acknowledge that the actual risks to human health stemming from the use of antimicrobials in food-producing animals remains an unresolved scientific issue.[5] While the literature in Canada and other countries consistently reports that antimicrobial-resistant bacteria are finding their way into the human food supply via animal-based food products (see Appendix C for examples), quantifiable impacts on human health have not been clearly established.

A number of studies that have examined the impact of Denmark's ban (imposed in 2000) on the use of antibiotics for purposes of disease prevention and growth promotion in pork, poultry, and cattle production have found that the ban has had no impact on human health, although it has had economic consequences. For example, Hurd (2012) found that while the economic costs of the ban were great, the public health did not improve. Over the 10-year period since the ban was introduced, salmonella and campylobacter illness rates did not decrease; MRSA increased steadily; and resistance levels in some key human infections increased. Furthermore, the use of antibiotics for therapeutic purposes increased over the period examined. The study concluded that evaluation of risks of individual antibiotics within the context of their actual use is preferable over a broadly-based ban.

Likewise, Bender (2011) found that despite an overall reduction in the tonnage of antibiotics used in Danish pork production, the use of therapeutic antibiotics increased; the costs of production increased; and the policy had negative impacts on the health of weaned pigs. The

[4] The use of antimicrobials for growth promotion and prophylaxis is estimated to account for 80% of antimicrobial use in agriculture in the US (Palmer et al., 2011, p. 4), and a majority of the use of these agents in Canada (CCAR, 2009, p. 22).

[5] It is also important to acknowledge the uncertainty in the literature regarding the relative contribution of agricultural antimicrobial use to AMR compared to clinical use, and the possibility that antimicrobial use in companion animals may also be contributing to AMR.

study also found that the number of human isolates that are resistant to medically important antibiotics has continued to increase in non-travelling Danish residents. Like Hurd, Bender concluded that a complete ban on antimicrobial growth promoters is likely not necessary and may create additional problems. Palmer et al. (2011) report that in spite of the Danish ban on the use of antibiotic growth promoters in agriculture, there has been no discernible decrease in AMR (p. 5).

On the other hand, Danish scientists report that total antibiotic usage per kilogram of pork decreased by more than 50% between 1992 and 2007, while total Danish pig production increased by 43%, and the average number of pigs produced per sow per year increased from 21 to 25 (Aarestrup & Wegener, 2009). However, since 1999, the use of antimicrobials in swine has increased, due in part to the emergence and spread of new infectious diseases; weaner mortality increased between 1993 and 2003, but, as of 2009, had been reduced to pre-ban numbers; and finisher mortality slowly increased between 1993 and 2007. The authors conclude that "discontinuation of non-therapeutic antibiotic use has not negatively impacted long-term swine productivity in Denmark."

In a Canadian context, some stakeholders involved in consultation on development of a Canadian risk management strategy on AMR have warned that banning growth promotants could result in reduced meat quality, increased use of antimicrobial agents for therapeutic purposes, increased costs for producers and consumers, and/or consequences for trade (VDD, 2003a, pp. 7–8). The Danish experience suggests that increased therapeutic use of antimicrobials is a real possibility.

**Direct exposure to veterinary drugs (handler safety)**

Human health can also be affected adversely by direct exposure to some veterinary medicines, though this perhaps is a less significant risk. For example, in 2003 and 2004, the VDD released notices to hospitals and veterinarians warning that accidental self-injection by human beings with the antibiotic Micotil® had been associated with potentially fatal human health outcomes (Health Canada, 2003a, 2004a). Another example is clenbuterol, which can be used to manage chronic obstructive pulmonary disease (COPD) in horses (Lust, Barthold, Malesker, & Wichman, 2011), but which is currently prohibited in Canada for sale for administration to food-producing animals, as noted above (VDD, 2009a). In addition to the threat of exposure through veterinary drug residues (described above), individuals have been known to experience adverse health impacts affecting the heart and central nervous system after deliberately exposing themselves to clenbuterol (Lust et al., 2011, p. 202).[6]

As the above discussion suggests, although veterinary medicines are important for protecting animal and human health, in some circumstances, these products could have the opposite effect. Given the potential human health implications of veterinary drug use, as well as the ongoing scientific uncertainties particularly in relation to AMR, findings from the literature review suggest an ongoing need for regulatory intervention in this area.

[6] Clenbuterol is used for its performance enhancement and weight loss attributes.

### 4.1.2 Alignment with federal priorities

**The VDP is well-aligned with federal government priorities to protect Canadians from unsafe food and consumer products.**

The evaluation found the VDP to be aligned with the priorities of the Government of Canada. Although recent Speeches from the Throne (2006–11) and federal budgets do not specifically mention veterinary drugs as a priority, the Speech delivered on October 16, 2007, stated that the federal government "shares the concern of parents about the safety of consumer products and food," promising that it would "introduce measures on food and product safety to ensure that families have confidence in the quality and safety of what they buy" (GoC, 2007). Similarly, in the March 3, 2010, Speech from the Throne, the government vowed to "reintroduce legislation to protect Canadian families from unsafe food, drug and consumer products" (GoC, 2010) and to strengthen Canada's food safety system. Thus, although there is no Speech material specifically devoted to veterinary drugs and it is unclear specifically what legislation the federal government was referring to in its 2010 Speech, the VDP relates closely to the federal priorities identified in these recent Speeches from the Throne.

Following up on the intentions expressed in the 2007 Speech, the federal government introduced the Food and Consumer Safety Action Plan (FCSAP) in 2008. The FCSAP is a five-year, $489.4 million horizontal initiative between Health Canada, the PHAC, the CFIA, and the Canadian Institutes of Health Research (CIHR) whose stated objective is "to protect the health and safety of Canadians by ensuring the safety of health and consumer products and food" (Health Canada, 2008a, p. 5) by implementing a modernized safety regime which incorporates active prevention, targeted oversight, and rapid response to identified risks in food, health, or consumer products (2008a, p. 1).

Veterinary drugs are implicated in one of 11 strategies under the Health Products component of the Food and Consumer Safety Action Plan (FCSAP), namely Strategy #10: Risk-based Border Integrity Initiatives. Strategy #10 involves the development of a national program to increase coordination and collaboration between Health Canada and the CBSA, with the objective of protecting Canadians from using or consuming non-compliant imported health products. It is unclear why veterinary drugs did not receive funding under the other 10 FCSAP strategies, since at least some of them are relevant to veterinary drugs.[7]

Although the interviews did not include a specific question on the relative priority given by Health Canada to veterinary drugs versus other health products, a few key informants observed a tendency within Health Canada to prioritize human drugs over veterinary drugs. They noted that regulatory changes pertaining to veterinary drugs often are not discussed until analogous changes have been made on the human side and that, as a result, the specific issues and challenges relevant to veterinary drugs may be overlooked. These perceptions are lent some credence by the

[7] Under the Health Products component of the FCSAP, the other 10 strategies are: pre-submission meetings; pharmacovigilance planning; risk management and mitigation strategy; regulatory framework for APIs; interim funding to speed up drug approvals; consumer information strategy for health products; Periodic Safety Update Reports; mandatory adverse reaction reporting by institutions; Drug Safety and Effectiveness Network (involving post-market research and surveillance); and corrective action/fines and penalties.

exclusion of veterinary drugs from most FCSAP strategies, as well as their exclusion from Health Canada's recent regulatory amendments making Good Manufacturing Practices (GMPs) and Establishment Licences a requirement for active pharmaceutical ingredients (APIs) used in human drugs in Canada, which will come into force in the fall of 2013 (Health Canada, 2013). APIs used exclusively in veterinary drugs are excluded from these regulations.

Veterinary drugs are included in federal government's Growing Forward Framework Agreement. Under the Agreement, enhanced safety and security of the food system will be achieved through three related initiatives, including food safety systems development, recognition, and implementation (AAFC, 2008, p. 28). Within Growing Forward, the Veterinary Drugs Initiative is also expected to contribute to a competitive and innovative agricultural sector in Canada by, among other things, increasing scientific capacity to review veterinary drug submissions and by streamlining generic veterinary drug approvals (AAFC, 2008, p. 14). Given that approval for veterinary drug submissions is one of the VDP's main business activities, the inclusion of an initiative relating to veterinary drug approvals in Growing Forward suggests strong alignment between the VDP and current federal government priorities.

Finally, the VDP aligns with Health Canada's current Program Activity Architecture (PAA) and, in particular, with the strategic outcome focussed on ensuring that Canadians "are informed of and protected from health risks associated with food, products, substances and environments, and are informed of the benefits of healthy eating," and "to [thereby] ensure that the food that Canadians eat and products they use are as safe as possible, and that threats to health are addressed effectively" (Health Canada, 2012a, p. 25).

### 4.1.3 Consistency with federal roles and responsibilities

**The VDP is consistent with federal roles and responsibilities, as expressed in federal legislation and regulations.**

The evaluation also found the VDP to be consistent with federal roles and responsibilities. Aspects of the VDP relating to human health align closely with Health Canada's responsibilities under the *Department of Health Act* (1996). Under the Act, the Minister's duties involve "all matters over which Parliament has jurisdiction relating to the promotion and preservation of the health of the people of Canada not by law assigned to any other department, board or agency of the Government of Canada" (GoC, 1996, sec. 4(1)). The roles the Department (now known as Health Canada) is required to fulfill include promoting the physical, mental, and social well-being of people in Canada; protecting them against health risks; conducting investigations and research in public health, including monitoring diseases; establishing consumer product safety standards; and collecting and distributing health-related information (GoC, 1996, sec. 4(2)).

Health Canada's role in the delivery of the VDP is further delineated by the *Food and Drugs Act and Regulations*. Veterinary drugs are included in the Act's definition of a drug as "any substance or mixture of substances manufactured, sold, or represented for use in:

a) the diagnosis, treatment, mitigation or prevention of a disease, disorder or abnormal physical state, or its symptoms, in human beings or animals;
b) restoring, correcting, or modifying organic functions in human beings or animals; or

c) disinfection in premises in which food is manufactured, prepared, or kept" (GoC, 1985, sec. 2).

The Act provides the legal basis for Health Canada's regulatory role related to drugs, which extends to labelling and packaging; size, dimensions, and specifications; standards of composition and purity; the conditions of sale; and the use of any substances as ingredients (1985, sec. 30). In addition, the Act gives authority to Health Canada to set and enforce regulations regarding the objects of the Act, and contravening the regulations is a punishable offence (1985, sec. 30–36), aligning with the compliance and enforcement aspects of the VDP.

Health Canada shares legislative and regulatory responsibility for veterinary drugs with the CFIA and the provinces and territories. The CFIA has responsibilities under the *Food and Drugs Act* in the enforcement of regulations over veterinary drugs, and is also responsible for the enforcement and administration of the *Feeds Act and Regulations* and the *Health of Animals Act and Regulations*. The CFIA is responsible for regulating feeds under the former and veterinary biologics under the latter.

Finally, the use of veterinary drugs falls within provincial/territorial jurisdiction. Thus, while Health Canada is responsible for evaluating the safety and efficacy of new veterinary drugs, it has no regulatory authority over the use of veterinary drugs or the practice of veterinary medicine or pharmacy. However, it can influence use indirectly through other channels, such as product labelling and the preparation and dissemination of risk information.

## 4.2 Program governance

**Historically, no single entity has had formal authority for governing the VDP. However, a variety of formal and informal mechanisms and structures have been in place to govern aspects of VDP activity. With recent changes to HPFB's governance structure, the VDP is considered part of the larger Pharmaceutical Drugs Program, which also includes human drugs.**

The VDP includes all activities undertaken by the VDD, as well as relevant activities conducted by the Inspectorate/RAPB and the CFIA. Based on the document review, there is no evidence that, historically, any single body has managed or coordinated the activities undertaken by these groups or has had overall authority for the VDP. This may be because the veterinary drug-related activities of Health Canada and the CFIA, historically, have not been conceptualized as a "program."

Within HPFB's new governance structure, implemented in 2012–13, veterinary drugs have been conceptualized as part of HPFB's Pharmaceutical Drugs Program (HPFB, 2012a). The Pharmaceutical Drugs Program also includes human drugs, and is governed by a Program Executive Committee Sub-Committee. Similar Sub-Committees exist to govern the Biologics, Medical Devices, Natural Health Products, Food Safety and Nutrition, and Nutrition Policy and Promotion programs.

While-there is no clear evidence that the absence of a coordinating body focused on veterinary drugs has had detrimental consequences for the delivery of Health Canada's veterinary drugs-related activities, this is not to say that benefits would not be derived from greater coordination among the program partners. In the absence of a coordinating body for veterinary drugs activities, there are a variety of formal and informal mechanisms and structures in place to govern various aspects of VDP activity.

### Collaboration among Health Canada partners

Within Health Canada, program documents show that the VDD and the Inspectorate collaborate in a variety of ways relating to compliance and enforcement of the regulatory framework for veterinary drugs. Some examples include sharing information relating to adverse reactions, compliance verifications, and complaints; collaborating on the development and issuance of communications products; and holding discussions on compliance and enforcement-related issues, new inspection approaches, and proposed legislative and regulatory changes. On a case-by-case basis, the VDD conducts HRAs in response to requests by the Inspectorate, and provides the Inspectorate with recommendations for regulatory action.

### Collaboration between Health Canada and the CFIA

Health Canada and the CFIA also collaborate to deliver VDP activities in a variety of ways. Overall, interviewees representing the VDD and the CFIA agreed that their organizations have a long-standing and positive relationship. It was reported that although Health Canada and the CFIA previously had a joint management committee that met monthly for many years to discuss issues related to veterinary drugs, the two organizations now meet only as specific needs or issues arise. That being said, the CFIA and Health Canada both participate in the regular meetings of the Canadian Animal Health Products Regulatory Advisory Committee (CAHPRAC), which was established in early 2008 by the two organizations in association with the CAHI, the main Canadian industry association for veterinary drugs (VDD, 2009b, p. 1).

In the area of veterinary biologics, the VDD and the Canadian Centre for Veterinary Biologics within the CFIA have a Memorandum of Understanding that clarifies the division of responsibilities between the two agencies by identifying what products are considered veterinary biologics and drugs, respectively (CFIA & Health Canada, n.d.). The MOU specifies that if a product invokes a specific immune response for an infectious disease, it is considered a biologic and falls within the CFIA's authority. Conversely, if a product stimulates an immune response to a non-infectious disease, generally it falls within Health Canada's mandate. Health Canada key informants noted that because veterinary technologies are becoming more complex and sophisticated, the line is blurring between Health Canada's and the CFIA's responsibilities, and consultation between the two agencies is often required to determine which agency has regulatory authority or whether a review should be done jointly. They reported that a working group devoted to the classification of veterinary drugs and biologics has recently been formed, and a list of classification criteria is in development. An updating and revising of the MOU is also currently under consideration.

In addition, Health Canada key informants reported that since adverse reaction reporting requirements are in place for both biologics and other veterinary drugs, Health Canada and the CFIA recently began collaborating to develop a shared database that would allow companies to

submit adverse reaction reports electronically; depending on the product, the information would go to either Health Canada or the CFIA. This initiative is intended to eliminate potential confusion on the part of veterinarians and others reporting adverse reactions, who may not know which organization is responsible for different classes of products.

In the area of feeds, the VDD and the Animal Feeds Division of the CFIA also collaborate, because of overlap in the definitions for a "drug" in the *Food and Drugs Act* and a "feed" in the *Feeds Act*, to determine the regulatory status of individual products found in the field (Health Canada, 2011b, pp. 17–18). This arrangement does not appear to be formalized through an MOU or similar agreement such as the one that is in place to distinguish between veterinary drugs and biologics. However, a VDD-CFIA working group is currently developing a guidance document to help industry delineate between a drug and a feed (2011b, p. 18). The VDD and the CFIA also collaborate on the joint Health Canada–CFIA Drug Carryover Residue Risk Ranking Project, the intent of which is to rank the risks of feed-borne drugs to non-target species. The objectives of the project are to revise the CFIA drug sequencing guide to allow drug/species combinations identified as being low risk, and identify where additional controls may or may not be required as part of the Medicated Feeds Regulations (Health Canada, n.d.).

The VDD and the CFIA's Food Safety and Consumer Protection Directorate collaborate with respect to veterinary drug residues in food. While the VDD is responsible for establishing MRLs, the CFIA is responsible for monitoring compliance with established MRLs through its inspection program, and for taking appropriate risk management actions. In addition, Health Canada representatives indicated that the VDD liaises with the Food Safety Science Branch on issues related to methodology for veterinary drug residues, and provides advice, as needed, to specific Program areas within the CFIA (e.g., Fish and Seafood, Red Meat, Egg, Honey).

Finally, the CFIA may submit requests for HRAs to the VDD,[8] or may communicate with the VDD or the Inspectorate with respect to specific issues, such as use of unapproved drugs or banned drugs, identified or arising through the course of its inspection activities.[9]

A few external key informants recognized that increased consultation and collaboration has been occurring between the VDD, the Canadian Centre for Veterinary Biologics (CCVB), and the AFD. These interviewees emphasized the need for a unified approach to address food safety issues and encouraged ongoing collaboration between Health Canada and the CFIA in this regard.

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8 For a summary of HRA requests and completed HRAs, please see Appendix C.

9 The CFIA provided the evaluation with extensive documentation of its communications with Health Canada in relation to issues identified through the course of its inspection activities, such as the sale, prescribing, use and/or compounding of unapproved drugs, active pharmaceutical ingredients, and even banned drugs, including their use in livestock feeds. These communications clearly indicate that the CFIA informs Health Canada of activities that appear to contravene the *Food and Drugs Act* and Regulations, and requests clarification, advice, and/or enforcement action. Although the documents also include Health Canada's responses, it was beyond the scope of this project to complete a thorough analysis of the communications.

### Collaboration with other federal departments and agencies

In addition to collaborating with VDP partners, Health Canada also collaborates with various other federal departments and agencies on veterinary drug-related activities.

As part of the FCSAP, the Inspectorate works with the CBSA to implement FCSAP activities related to health products, including veterinary drugs, through the Border Integrity Program (Health Canada, 2008a, p. 7, 2011b, p. 4). Health Canada key informants reported that discussions have also been held with the CBSA related to tracking veterinary drugs entering Canada under the own-use importation (OUI) provision of the *Food and Drugs Act*, although they also reported that these discussions did not result in any agreement to collaborate.[10]

The VDD has an MOU with PHAC's Laboratory for Foodborne Zoonoses to administer the CIPARS and to enhance the exchange of information on AMR surveillance data needed for risk assessment, risk management, and policy development on AMR (VDD & PHAC, 2005). The VDD contributes to CIPARS through pre- and post-market evaluations, and provision of technical and financial support (Health Canada, 2011b, p. 4). The CFIA also has responsibilities within CIPARS, including product sampling and provision of cultures to PHAC for susceptibility testing.

More recently, Health Canada key informants reported that Health Canada has begun working with PHAC (the lead federal agency for antimicrobial resistance, or AMR), the CFIA, AAFC, and the provinces and territories to develop a more coordinated approach to AMR. According to key informants, an interdepartmental science policy team on foodborne AMR has been newly created within the last six months. The team aims to provide leadership on federal and provincial/territorial efforts on foodborne AMR risk management, and to develop strategic, coordinated approaches to address the emergence and spread of foodborne AMR associated with non-human use of antimicrobials drugs.

Health Canada also collaborates with AAFC in carrying out the Veterinary Drugs Initiative as one element of the Growing Forward Agreement. This collaboration is formalized in an MOU between the two departments (AAFC & Health Canada, 2009). Noting that the pre-existing regulatory framework was perceived as needing improvement to support innovation in agriculture, as well as the competitiveness of the livestock sector, the MOU pledges to address these concerns "through plans for closer harmonization of technical requirements for veterinary drug approvals and a timelier and more transparent process to improve the sector's competitiveness by increasing the availability of newer and more effective drugs to Canadian livestock producers" (AAFC & Health Canada, 2009, p. 3).

Health Canada key informants reported that the VDD has an MOU with the Pest Management Regulatory Agency (PMRA), the purpose of which is to differentiate between pesticides and veterinary drugs. They also reported that the two organizations share best practices on topics such as parallel review and international harmonization. In addition, key informants reported that the VDD is exploring an approach that the PMRA has implemented to address situations where the private sector lacks financial incentive to submit needed pesticides for regulatory approval.

[10] Own-use importation is discussed in detail in Section 4.3.2.

To address the issue, PMRA established the Pest Management Centre under AAFC to collect the necessary data to support submission. Health Canada key informants reported that the VDD is considering whether a similar approach could be taken to address similar problems relating to minor use, minor species (MUMS) drugs.[11]

Finally, Health Canada representatives reported that the VDD works with the Department of Fisheries and Oceans (DFO) in relation to aquaculture, and with the Department of Foreign Affairs and International Trade (DFAIT) in case of any trade dispute as it relates to veterinary drug residues.

### 4.2.1 Performance measurement

**Revisions to the existing logic model and performance measurement strategy for the VDP would ensure consistency with Health Canada's mandate, Branch-level frameworks and tools, and the objectives of regulatory modernization, as well as the capacity to support future evaluations of the VDP. Despite the inclusion of the VDP in the larger Pharmaceutical Drugs Program, it is important for Health Canada to retain the capacity to continue reporting separately on veterinary drugs activities and outcomes.**

Performance measurement strategies have been developed for the FCSAP (Health Canada, 2008a) and for the Veterinary Drugs Initiative under the Growing Forward Agreement (AAFC & Health Canada, 2009), and associated performance reporting is taking place. To date, three annual performance reports have been produced for the FCSAP, and one has been produced for the Veterinary Drugs Initiative (Health Canada, 2010c, 2010d, 2011c; VDD, 2009c). However, in the case of the FCSAP reports (Health Canada, 2010c, 2010d, 2011c), veterinary drugs are mentioned only in passing.

Additionally, some performance information is available in VDD and Inspectorate reports, although this data is primarily activity and output-based, and therefore is of limited value in assessing the extent to which outcomes have been achieved. On the other hand, at least some of this performance information is evidently used to inform decision making. For example, timely screening and review of veterinary drug submissions has been a central preoccupation of the VDD over the evaluation period, and regulatory operational performance (i.e., status of drug submission reviews) was being tracked as early as 2002–03 (VDD, 2003b, pp. 4–6). VDD key informants reported that performance information is used to inform decision making in the following ways:

- Drug submission status is used in monthly workload management forum meetings, the purpose of which is managing the drug submission workload.
- Pharmacovigilance data and CIPARS data are used by drug reviewers when reviewing drug submissions.
- A semi-annual special management committee meeting evaluates performance and considers actions for the coming year.

[11] MUMS is discussed in detail in Section 4.3.2.

Most recently, reporting on some veterinary drug-related activities and outputs has been included in HPFB's integrated dashboard reports. These reports were introduced as a result of the implementation of a new framework for cost recovery for drugs for human use and medical devices in April 2011. The reports are used to inform decisions on priorities and resource allocation. The July 2013 integrated dashboard report, for example, included data on the number of veterinary drug submissions, adverse reaction reports, and PSURs received, as well as data on submission review performance for veterinary drugs. It is unclear what impact HPFB's new governance structure will have on performance measurement related to veterinary drugs. As already noted, under the new structure, veterinary drugs have been conceptualized as part of the larger Pharmaceutical Drugs Program. However, the issues relevant to veterinary drugs are in many ways unique, necessitating a distinct regulatory approach.-Health Canada's ongoing work to develop a separate veterinary drugs regulatory framework recognizes the uniqueness of these products. In any event, it is important from an accountability perspective that Health Canada retain its ability to report on both the outputs and the outcomes achieved of its regulatory activities related to veterinary drugs.

## 4.3 Program implementation

The evaluation found that the VDP has made progress over the evaluation period in implementing its planned activities and, in the process, has responded to several emergent issues and challenges. Nevertheless, a number of important issues and challenges remain. Below, the VDP's progress is described in relation to its six main activity areas: research and surveillance; regulatory and policy development; pre-market activities and standard-setting; post-market surveillance; compliance and enforcement; and communications and stakeholder engagement.

### 4.3.1 Research and surveillance

**While the VDP has carried out some research and surveillance activities, these are relatively limited in comparison to the work it has undertaken in other areas.**

According to the VDP logic model, this activity consists of research and surveillance intended to enhance sound policy and regulatory development. Examples might include research into drug residue detection methodologies, residue monitoring, and surveillance of antimicrobial resistance. According to Health Canada, research into residue monitoring is done by the CFIA, as is the majority of research into residue detection methodologies; research into surveillance of AMR was initiated by Health Canada but is now being led by PHAC, with Health Canada's support.

Over the evaluation period, Health Canada has carried out several research and surveillance activities, including contributing financially towards the creation and maintenance of CIPARS (2002 to present); analyzing CIPARS results and reviewing CIPARS reports (2003 to 2011); funding research activities at the Food Directorate on veterinary drug residues (2003 to 2006); and collaborating with international organizations on research projects relating to BSE/TSE. These activities appear relatively limited in comparison to the work that Health Canada has

undertaken in other main activity areas identified above. However, without understanding the level of funding allocated to this activity relative to others, it is difficult to assess Health Canada's efforts in this area.[12]

### 4.3.2 Regulatory and policy development

**The VDP has taken steps to address several inter-related issues through regulatory and policy development. These include developing a policy for extra-label drug use; introducing initiatives to increase access to veterinary drugs for minor use, minor species; taking steps to address antimicrobial resistance; and introducing a streamlined application process for veterinary natural health products. The VDP has recently started to address aspects of the regulatory framework that permit the importation and use of unapproved veterinary drugs and current policies that permit importation of active pharmaceutical ingredients, which are largely unregulated by Health Canada.**

Regulatory and policy development is a key activity under the VDP. Over much of the evaluation period, this activity has taken place within a context of broader regulatory modernization for health products being undertaken by HPFB. The Branch's plans for regulatory renewal were articulated in the 2007 Blueprint for Renewal document (HPFB, 2007a) and, more recently, in the Regulatory Roadmap for Health Products and Food, released in May 2012 (HPFB, 2012b). The broad goals of regulatory renewal, as expressed in these strategic planning documents, include the following:

- taking a "product lifecycle" approach to regulation, i.e., an approach to regulating health products that encompasses all stages of product development;
- implementing regulatory interventions proportional to risk;
- strengthening post-market surveillance and compliance and enforcement;
- learning from and collaborating with international counterparts;
- enhancing transparency and openness;
- basing regulation on scientific evidence; and
- ensuring the sustainability of the regulatory framework.

In relation to veterinary drugs, the Regulatory Roadmap articulates plans to propose a new separate regulatory framework for veterinary drugs aimed primarily at ensuring the safety of the food supply and "based on the premise that the degree of control exercised over various products should be proportional to the level of harm they present" (HPFB, 2012b, p. 19). In January and March 2013, pursuant to this modernization initiative, Health Canada held consultations with stakeholders with the objective of outlining, for discussion and exploration, possible approaches being considered by the Department. The consultations addressed all stages of the product life cycle — including pre-market review, post-market surveillance and monitoring, and compliance and enforcement — as well as specific issues such as oversight of importation, minor use, minor species (MUMS) access to veterinary drugs in exceptional circumstances, environmental assessment for veterinary drugs, and others.

[12] See Economy and Efficiency section for a more fulsome discussion on program funding.

With that context in mind, the discussion below identifies several key interrelated issues that have required Health Canada's regulatory and policy attention over the evaluation period. Overall, it is clear that the VDP has taken steps to address some of these issues, but despite substantial progress in many areas, a number of unresolved issues and challenges remain. Health Canada key informants reported that regulatory reform is expected to resolve some of these issues and challenges by addressing some of the shortcomings of the existing framework. That being said, they also observed that there are numerous challenges to regulatory reform, including the complexity of issues involved, shared jurisdictions and responsibilities, and the potential economic impacts of regulatory reform for Canadian agriculture.

**Use of unapproved drugs**

The use of veterinary drugs that have not been approved by Health Canada has been a major issue for the VDP over the evaluation period. Such use stems from two features of the current regulatory framework for veterinary drugs:

- Current regulations permitting importation of unapproved drugs for use on animals. There is currently no prohibition against the importation of unapproved drugs for use on animals. Furthermore, Canada's Import and Export Policy for Health Products under the *Food and Drugs Act* and its Regulations (POL-0060) states that individuals returning from abroad may bring with them a single course of treatment or a 90-day supply of a health product for themselves, another person, or "for use on an animal for which they are responsible and with whom they are travelling" (Inspectorate, 2010a, p. 5). Originally conceived to enable continuity of care for humans, the OUI provision has been used by livestock producers to acquire less expensive veterinary products or products not available in Canada, from the US and from other countries, for use in their livestock operations (Handa & Webster, 2009; OUI Task Force, 2008).
- Current policies relating to APIs. Under current regulations, APIs can be legally sold or imported as raw materials for further modification; they are not subject to labelling regulations or Drug Identification Number (DIN) requirements, and are not intended to be used as drugs in dosage form (Inspectorate, 2007a). Nevertheless, bulk APIs are being imported, manufactured, sold and represented for use as veterinary drugs in dosage form, which Health Canada has noted in its *Policy for the Importation or Sale of Active Pharmaceutical Ingredients for Veterinary Use (POL-0018)* "avoids the controls of the Canadian drug regulatory system, impacts the safety of the domestic food supply, affects the availability of high quality veterinary drugs in Canada, and may have impacts on the export of food products" (Inspectorate, 2007a).

Representatives of the animal health products industry strongly support restrictions on OUI and APIs, estimating that unlicensed drugs presently account for about 20% of the total Canadian animal health market (CAHI, 2007, p. 11). In one recent report, CAHI argues that "it is inconsistent for regulatory authorities to hold ethical animal health companies to stringent standards while no standards are applied to non-approved imports for own-use and APIs" (p. 11). In that same report, CAHI recommends that Health Canada harmonize its approach to importation and use of unlicensed veterinary drugs with other jurisdictions, which would involve

prohibiting importation and use of unlicensed drugs, and restricting importation of bulk chemicals and APIs to holders of Establishment Licenses (p. 11).[13]

More recently, the 2011 International Federation for Animal Health's (IFAH) Global Benchmarking Survey for Canada found "overwhelming disappointment" among the Canadian animal health product industry with the failure of regulatory authorities to curb the "expanding unapproved product market" by curbing OUI, importation of APIs, and API compounding (BioBridge Ltd, 2012, p. 4). Among a series of wide-ranging recommendations, the report recommended "as a first priority" finding answers to the continuing problems of unapproved products, OUI, and API abuse (BioBridge Ltd, 2012, p. 5).

On the other hand, producer representatives have argued that restricting OUI would affect the competitiveness of Canadian producers by driving up the cost of production, and have suggested instead acting to address the price differentials between drugs available in the US and Canada (AGRI, 2008, p. 10).

Clearly, there are strong views on both sides of the issue among those with an economic interest at stake. Among experts in the field there is concern that OUI, including importation of antimicrobial APIs, may be a contributing factor to increased AMR in food-producing animals. For this reason, the Advisory Committee on Animal Uses of Antimicrobials and Impact on Resistance and Human Health (2002) recommended regulation 10 years ago to curb OUI of antimicrobials and antimicrobial APIs in Canada. More recently, a conference on antimicrobial stewardship in Canada in late 2011 concluded that resolution of regulatory issues around OUI should be one of the priorities in promoting antimicrobial stewardship in food animal production (Prescott, Szkotnicki, McClure, Reid-Smith, & Léger, 2012, p. 19).

Health Canada has acknowledged the potential public health impacts associated with the use of unapproved drugs and has considered regulatory approaches to managing the issue.

- Health Canada held stakeholder consultations on a proposed regulatory amendment to prohibit the importation of unapproved drugs destined for use in food-producing animals between November 2, 2004, and January 1, 2005 (Health Canada, 2005a). A summary document prepared by Health Canada in response to concerns expressed by stakeholders noted that the VDD was "participating in Health Canada's Canadian Health Protection Legislative Renewal initiative, which includes…a complete review of Personal Use importation of veterinary drugs." In response to concerns about the potential costs to Canadian livestock producers of a prohibition on OUI, the VDD noted that "[w]hen taking into consideration risks to human health, public safety and animal health, the cost advantage is not a sufficient reason to permit the importation of unapproved veterinary drugs".
- In a 2005 Issue Analysis Summary (IAS) prepared as part of Health Canada's general legislative renewal efforts, the VDD again observed that importation and/or inappropriate use of veterinary health products by producers could potentially threaten public health, thereby

[13] For example, unlicensed drugs may be legally imported into the US only if the consignee holds a specific exemption, and bulk APIs may only be imported for further manufacturing and/or processing if the importer has approval for the veterinary drug or medicated feed premix into which the bulk APIs are to be processed (CVM, 2011a).

warranting restrictions over these practices (VDD, 2005a, pp. 5–6). However, notwithstanding the fact that stakeholder consultations had already been held by that time on a proposed regulatory amendment to prohibit OUI, none of the regulatory changes proposed in the IAS actually sought to restrict this practice.

- In 2007, Canada established an OUI Task Force to examine the issue of personal importation of veterinary drugs and to develop recommendations to address the situation. In its final report, the Task Force recommended piloting a Restricted Import Permit Program (RIPP), which would have involved closing current OUI provisions while enabling producers to import specific eligible veterinary products after submitting an application to the VDD (OUI Task Force, 2008). However, beyond agreeing on the need for regulatory reform in the area of veterinary drugs and biologics, there was little consensus among members of the OUI Task Force on the way forward.[14]

VDD representatives reported in interviews that the new regulatory framework for veterinary drugs will address OUI and APIs, among other issues. These topics were among several included in stakeholder consultations held in March 2013. During these consultations, the VDD put forward for consultation a "flexible regulatory structure to allow access to unapproved veterinary products" that would include the elements identified (see below).

**Proposed elements of new regulatory framework for APIs and OUI**

APIs

- Limiting importation of APIs to establishment licence holders
- Considering importation of APIs for sale to feed mills, retailers, farmers, or other end-users as the sale of a drug in dosage form, and therefore subject to compliance with the *Food and Drug Regulations* with respect to marketing authorization, GMPs, establishment licensing, and labelling requirements
- Making GMPs compulsory for all APIs for veterinary use through adoption of ICH Q7 Guidelines concerning GMPs for human use APIs

OUI

- Establishing eligibility criteria for products for OUI that meet the objectives of food safety, including:
    - Only OTC drugs
    - Only formulated products in final dosage form
    - No Category I, II, or III medically-important antimicrobial drugs

[14] It is unclear if the RIPP was ever implemented. VDD performance reporting for 2010–11 notes that under the current regulatory framework, a Controlled Permit program for managing OUI would be voluntary, adding that "all stakeholders agree that a regulatory revision is required to resolve the issue," but that "there is still divergence of opinion as to which regulatory amendments are acceptable" (HPFB, 2011a). In particular, some stakeholders were opposed, for economic reasons, to closing the border to OUI.

  - Product must be approved by a recognized foreign regulator
  - The product could only be imported into Canada directly from the country of the recognized foreign regulator
  - Must contain the identical active ingredient to an approved Canadian product with an active DIN
  - Must have a Canadian MRL already established or a status of no MRL required in the species under consideration
  - Drug is not under re-evaluation in the foreign country where it is approved
  - Drug is not under patent or data protection
- Requiring an application for an import permit for drugs that meet the eligibility criteria

Source: (VDD, 2013a)

As noted above, in the fall of 2013, regulations making GMP and Establishment Licenses a regulatory requirement for APIs in Canada, and imposing traceability requirements, will come into force. However, these regulatory amendments pertain only to drugs for human use; APIs included solely in drug products for veterinary use are not within the scope of the Regulations (GoC, 2012b). Under the changes proposed by the VDD in March 2013, GMPs would become mandatory for all APIs for veterinary use. However, VDD representatives emphasized that any regulatory changes will depend on feedback received from stakeholders on its proposed approach.

## Extra-label drug use (ELDU)

An issue related to the use of unapproved drugs is ELDU, which Health Canada defines as the "use or intended use of a drug approved by Health Canada in an animal in a manner not in accordance with the label or package insert (VDD, 2011a). ELDU may be appropriate in cases where there is insufficient incentive on the part of veterinary drug manufacturers to produce drugs for particular conditions in particular species, or where existing products are not expected to be effective (Health Canada, 2011d). While this may not be ideal, in many cases veterinary professionals can make reasonable inferences about drug efficacy and safety on the basis of experience in other settings and, in any event, no other alternatives may exist (Rollin, 2002, p. 749).

However, there are public health concerns associated with ELDU. Aside from animal health concerns (e.g., adverse health events), these concerns include the presence of violative drug residues in animal-derived food products, and potential for the development and spread of AMR (ELDU Advisory Committee, 2004; Gehring, Baynes, & Riviere, 2006; Province of Manitoba, 2008). Such residues are perceived as a concern in the context of ELDU because the uses to which a particular drug is actually being put may differ from the uses whose associated risks authorities had assessed as part of the approval process. Moreover, the monitoring of drug residues is complicated by the unavailability of MRLs and Administrative MRLs (AMRLs) for drugs used in an off-label manner (ELDU Advisory Committee, 2004, p. 20; Gehring et al., 2006, p. 8). ELDU can also contribute to the emergence of antimicrobial-resistant pathogens capable of causing disease in humans, for example through the use of antimicrobials of high importance in human medicine but unapproved in food animals (Advisory Committee on Animal Uses of Antimicrobials and Impact on Resistance and Human Health, 2002, p. XII).

Although the use of veterinary drugs, including ELDU, comes under the practice of veterinary medicine – a provincial jurisdiction – these potential public health impacts of ELDU have prompted Health Canada to consider more regulatory oversight in this area. For example, in its 2005 Issue Analysis Summary the VDD suggested regulatory amendments requiring ELDU to be conducted under the supervision of a licensed veterinarian when it was expected to present a public health risk (VDD, 2005a, p. 19); as previously noted, the regulatory amendments proposed at that time did not proceed. More recently, in collaboration with an advisory committee established for this purpose, Health Canada published a policy for ELDU in food-producing animals (Health Canada, 2008b). Such a policy was first recommended by the Advisory Committee on Animal Uses of Antimicrobials and Impact on Resistance and Human Health (2002, p. XII).

Briefly, the policy on ELDU can be summarized as follows:

- ELDU is a recognized tool in veterinary medicine in the context of a valid Veterinarian-Client-Patient Relationship (VCPR).
- ELDU in food-producing animals is typically recommended only for licensed veterinarians.
- ELDU is not recommended with drugs of very high importance to human health (i.e., Category I antimicrobial agents).
- ELDU should only be undertaken in accordance with the *Food and Drugs Act and Regulations,* as these relate to banned substances, medicated feeds, and violative residues.

It is unclear if Health Canada's regulatory modernization initiative will introduce regulatory amendments relating to ELDU, such as the amendment proposed in 2005 that would have required ELDU to be conducted under the supervision of a licensed veterinarian when it was expected to present a public health risk. In contrast to Canada, the US *Animal Medicinal Drug Use Clarification Act* (*AMDUCA*), which was passed in 1994, stipulates that ELDU:

- must be undertaken by a veterinarian or in the context of a valid VCPR;
- is only appropriate when there is no efficacious, approved new animal drug labelled for a given use that contains the same active ingredient in the required dosage, form, and concentration;
- is limited to therapeutic uses (i.e., extra-label use for the purposes of production enhancement is prohibited);
- must not result in residues which present a risk to public health or which exceed safe levels, concentrations or tolerances; and
- is not permitted for animal feeds (CVM, 2011b).[15]

[15] Compounding, which is considered a form of ELDU in AMDUCA, is defined by the FDA as "the manipulation of drugs to obtain products that differ from the starting materials in an approved dosage form drug," and should be undertaken only from approved finished dosage form human and animal drugs and only if approved drugs used at approved doses and dosage forms are not appropriate (Comyn, 2003). Veterinarians and pharmacists are prohibited under AMDUCA from compounding unapproved veterinary drugs from APIs except for specific, rarely indicated antidotes (CVM, 2011b).

In the EU, legislation restricts ELDU to products for which MRLs or provisional MRLs have been established, or for which no MRL is necessary; specifies a *decision cascade* for ELDU that permits the use of human drugs in animal species only in rare circumstances; and clearly stipulates that ELDU should be exceptional and should only be undertaken to avoid "unacceptable suffering" by food-producing and companion animals (Alexander, 2005; European Commission, 2001 Articles 10-11; Gehring et al., 2006)

## Minor use, minor species (MUMS)

A relative lack of availability of drugs for minor uses and minor species has been another issue for the VDP over the evaluation period. According to a working definition prepared by the VDD, "minor uses" refers to small-scale (limited or infrequent) use of drugs in animals, while "minor species" refers to animals other than cattle, swine, chickens, turkeys, dogs, cats, and horses (AAFC & Health Canada, 2009, p. 9; Adewoye, 2005, p. 3), including, for example, fish, sheep, goats, bees, and zoo animals.

Scarcity of MUMS drugs occurs in part because the markets for these products are too small to enable the drug manufacturer to recoup the fixed costs associated with drug development, approval, and sale. In short, there may be insufficient return on investment from the manufacturer's standpoint to justify introducing MUMS drugs in Canada or other jurisdictions (Caswell, 2011, p. 4). Since there is no requirement on the part of drug manufacturers to address consumer needs, few MUMS drugs are commercially available (VDD, 2005a, p. 8).[16]

The inaccessibility of MUMS drugs can lead to potentially avoidable suffering by animals (Menzies, 2012), as well as increased reliance on ELDU, which, as already described, can affect human and animal health adversely (VDD, 2005a, p. 24). Increased prevalence of ELDU can sustain a vicious cycle whereby drug manufacturers are hesitant to introduce new MUMS drugs in Canada because demand in their target market is already being satisfied through off-label use of other products (Caswell, 2011, p. 4).

In the 2005 Issue Analysis Summary (IAS) prepared as part of general legislative renewal efforts, the VDD recommended addressing issues related to MUMS by being extended the authority to grant controlled access to veterinary drugs and by allowing manufacturers to sell these drugs with less stringent data requirements, depending on the level of risk they pose to human and animal health (VDD, 2005a, p. 24). Examples of requirements for the proposed regulations included providing legislative authority to Health Canada to consider data and reviews (or portions thereof) from other jurisdictions, promoting user-driven reviews, and making market approval conditional on manufacturers' commitments to produce the drug and monitor its safety and efficacy (VDD, 2005a, p. 25).

[16] Menzies (2012) observes that very few products are approved in Canada for goats, and none are available for lactating dairy sheep and goats (p. 51). Similarly, Health Canada (2007a) and the CFIA (2008b) have noted a dearth of available veterinary drugs for use in aquaculture and bees, respectively.

As mentioned earlier in this section, the amendments proposed in 2005 did not move forward. However, addressing the availability of MUMS drugs was one of the three elements of the Growing Forward Veterinary Drugs Initiative. The Initiative aimed to "help increase the availability and streamline the approval of drugs for MUMS, thus making it more cost effective for drug companies to file submissions in Canada" (AAFC & Health Canada, 2009, p. 24). This was to be achieved by: reviewing approaches to MUMS drugs in other jurisdictions and developing policy based on the findings of the review; generating a priority list of MUMS drugs in collaboration with industry; conducting a pilot MUMS approval project with the small ruminant sector; streamlining the MUMS submission review process; and producing policy, guidance documents, and MRLs for MUMS drugs (AAFC & Health Canada, 2009, p. 24).

While it is unclear if Health Canada has generated the priority list of MUMS drugs or produced MRLs for MUMS drugs, it has undertaken a number of initiatives to address MUMS, including the following:

- establishing an Advisory Committee on MUMS in 2005;
- drafting and completing consultations on a MUMS Policy Statement; although publication was planned for the end of 2011–12 (HPFB, 2011b, p. 6), to date this does not appear to have occurred; and
- implementing a specialized MUMS approval process.

Features of the specialized approval process include pre-submission consultations for drug sponsors to familiarize them with regulatory requirements for MUMS drugs; improved regulatory efficiency through international collaboration, including, but not limited to, acceptance of information from other jurisdictions; and flexible fee structures and "potential prioritization" (Caswell, 2011, pp. 3–4; Mehrotra, 2011). By the beginning of Q1 FY 2010–11, the first MUMS submission (for progesterone implants in sheep) had been completed, and a Notice of Compliance (NOC) had been issued (HPFB, 2010a, p. 9, 2011b, p. 3). This has been the only MUMS submission received by Health Canada to date; thus, the VDD did not reach its target under Growing Forward of five new MUMS drug submissions by March 31, 2013 (AAFC, 2013).

VDD key informants reported that, under the current regulatory modernization initiative, the Directorate is exploring potential ways of encouraging MUMS submissions in order to facilitate access to approved veterinary drugs for MUMS. In stakeholder consultations held in March 2013, the VDD outlined a proposed approach for putting forward a MUMS application involving pre-filing meetings between Health Canada and the sponsor to discuss the need for the product and the potential way forward; identification of evidence requirements and potential derogations from some evidence requirements (i.e., use of "alternative evidence pathways"); and conditional approval whereby market authorization is granted with the condition that additional data will be gathered and submitted to Health Canada over time (VDD, 2013b). The VDD also proposed that since most MUMS applications would be related to label expansion (e.g., adding species and indications to an existing label), producer groups or other third parties could initiate the application process, subject to the drug sponsor agreeing to amend the label should the third party provide satisfactory information in support of the expansion (VDD, 2013b).

The VDD's proposed approach is similar to that taken in the US under the *Minor Use and Minor Species Animal Health Act*, whereby a conditional approval process enables drug sponsors to market drugs for up to five years while collecting the necessary effectiveness data (although they must have already demonstrated that the drug is safe), while sponsors of designated drugs can apply for grants to support safety and effectiveness testing, and receive seven years of exclusive marketing rights on gaining approval or conditional approval (Center for Veterinary Medicine, 2012a). VDD representatives noted that the Directorate currently is seeking feedback on the proposed approach from stakeholders, and that the actual way forward will depend on the feedback received.

Finally, in the context of MUMS, it is also important to note that Health Canada has initiated some work in relation to aquaculture and the horse as a food-producing animal, but in both cases the evaluation had difficulty determining the current status of its work in these areas. With respect to aquaculture, the VDD established an Expert Advisory Panel (EAP) on Aquaculture in 2006 and conducted consultations on a proposed aquaculture policy document (VDD, 2007a). In the policy document, the VDD reported that it was undertaking the following activities in conjunction with the EAP to address the relative lack of drugs authorized for use in aquatic animal species:

- identifying drugs which are considered critical for the production of aquatic species;
- exploring partnership initiatives with provincial governments, members of the aquaculture industry, and academia;
- developing policy and guideline documents, including work to identify data requirements for veterinary drugs to be used in aquatic animal species;
- working with the industry to collect appropriate data to establish interim MRLs and withdrawal periods for drugs being used in aquaculture that have not yet received Health Canada authorization; and
- examining best practices in other regulatory jurisdictions.

By 2007–08, the EAP on Aquaculture had evidently been subsumed with the Advisory Committee on MUMS. In external interviews, it was suggested that the absence of a specialized MUMS program for aquaculture is a significant gap, while VDD key informants pointed out that the MUMS issue is not unique to aquaculture and therefore an aquaculture-specific policy or MUMS program is not necessary.

With respect to the horse as a food-producing animal, VDD performance reporting suggests that the VDD initiated a project on the horse as a food-producing animal and initiated a call for nominations for an Advisory Committee on the Horse as a Food Producing Animal. Growing Forward performance reporting for 2008–09 indicates that the VDD was drafting a discussion paper on a "Canadian approach to horse as a food-producing animal" at that time (VDD, 2009c); the evaluation could not determine if this has been completed.

Nevertheless, the VDD has worked with the CFIA and other stakeholders to develop and launch an action plan to address EU requirements announced in 2009 for horse meat importation (HPFB, 2010b), including requirements to identify horses for food production, introduce a tracking system and ensure that withdrawal periods are followed for veterinary medical products permitted to be used on horses that may be slaughtered for food. In response to a request by the

CFIA, the VDD provided information on non-permitted substances and essential drugs in equines and established a provisional withdrawal period for veterinary drugs in equines intended for food production (HPFB, 2010c). The CFIA's *Meat Hygiene Manual of Procedures* was updated accordingly (CFIA, 2011b). It is unclear what further policy and regulatory work is being undertaken by Health Canada in relation to the horse as a food-producing animal.

**Antimicrobial Resistance (AMR)**

As described in Section 4.1, there is general consensus in the literature that AMR is a serious threat to public health. While the role of veterinary medicine in the proliferation of resistant pathogens to which humans are exposed is a subject of current debate, the use of antimicrobial agents in food-producing and companion animals does contribute to AMR. Practices such as OUI and importation and use of APIs, along with other factors such as use of antimicrobial agents as growth promotants and ELDU, may be contributing to AMR.

AMR as it relates to use of veterinary drugs has been acknowledged by Health Canada as a serious concern for at least the past decade. In 2002, the Advisory Committee on Animal Uses of Antimicrobials and Impact on Resistance and Human Health, which was commissioned by Health Canada, issued a report with 38 recommendations targeting federal, provincial/territorial, and other partners and stakeholders to address the problem of AMR. The Committee's recommendations for Health Canada included the following:

- ensuring that regulation of antimicrobials (including licensing, sale, distribution, use, and regulatory compliance) includes consideration of the human health impact of AMR;
- developing specific methods and criteria for human and animal health safety assessment of veterinary drugs with respect to AMR;
- making all antimicrobials used for disease treatment and control available by prescription only;
- stopping direct importation of antimicrobial APIs;
- stopping the importation, sale, and use of antimicrobials not evaluated and registered by Health Canada; and
- developing an extra-label use policy that includes the ability to prohibit the extra-label use of specific drugs of critical importance to human health.

Although there has not yet been any policy or regulatory change related to OUI or APIs, Health Canada has addressed many of the Committee's recommendations relating to AMR. To date, the Department has done the following:

- incorporated consideration of AMR into the pre-market review of antimicrobials;
- developed a categorization of antimicrobials based on their importance in human medicine;
- since 2002, required all new antimicrobials to be available by prescription only;
- introduced label restrictions for ELDU of antimicrobials that are of very high importance in human medicine (fluoroquinolones and third generation cephalosporin products);
- required AMR risk management strategies to be included on product labels;
- reassessed the efficacy of existing antimicrobial growth promoters;
- led the Codex Intergovernmental Task Force on AMR; played a major role in developing Codex Guidelines on Risk Analysis of Foodborne AMR; and
- developed a policy on ELDU.

In contrast to Canada, the US has restricted the use of some antimicrobial agents at the national level, while the EU has phased out the use of antibiotic feed additives as growth promotants. Canada's response to AMR to date may also be seen as inconsistent with the 2011 recommendations of the WHO, which, as already noted, include terminating nontherapeutic use of antimicrobials, such as the use of antimicrobials as growth promoters; restricting or eliminating the use in food-producing animals of antimicrobials that are seen as critically important in human medicine; and requiring obligatory prescriptions for all antimicrobials used for disease control in food-producing animals.

Among external key informants who commented on the issue of AMR, many echoed the recommendations of the Advisory Committee on Animal Uses of Antimicrobials and Impact on Resistance and Human Health, urging Health Canada to take further action on AMR by addressing the OUI and API issues and making all antimicrobials available by prescription only, as well as by improving surveillance of AMR and use of antimicrobials. CIPARS is seen as a positive step forward in surveillance.

VDD representatives said that Health Canada is currently taking a number of additional steps to address AMR, including reviewing over-the-counter (OTC) products that belong to medically important antimicrobials to determine prescription status; working with the drug and feeds industry to phase out use of antimicrobial growth promoters for nontherapeutic reasons; and working with PHAC, the CFIA, AAFC, and provincial/territorial authorities to develop a more coordinated approach to AMR. As already noted, OUI and APIs are being addressed in the Directorate's current regulatory renewal efforts, which are expected to culminate in a separate regulatory framework for veterinary drugs.

## Veterinary natural health products (vNHPs)

One of the guiding principles of HPFB's regulatory modernization initiative, as expressed in the Blueprint for Renewal, has been to introduce regulatory interventions proportional to risk. To this end, Health Canada established an Expert Advisory Committee on Veterinary Natural Health Products in 2008 (EAC-vNHP) with a mandate to guide policy and program development relating to these products (EAC-vNHP, n.d.; VDD, 2011b). The EAC-vNHP has developed the following working definition of a vNHP: "a substance or mixture of substances administered across mucous membranes or applied topically and that is manufactured, sold, or represented for use in:

1. the diagnosis, treatment or prevention of a disease, disorder or abnormal physical state or its symptoms in animals; or
2. restoring, correcting or modifying organic functions in animals; or
3. articles intended to affect structure or function of the body in animals" (EAC-vNHP, 2010).[17]

[17] The EAC-vNHP's definition does not appear to include a description of the source materials of vNHPs, which presumably is one of the ways in which these products differ from other veterinary health products.

In addition, the EAC-vNHP defines "presumed safe products" as vNHPs that "are not likely to have a negative impact on the health of animals or the safety of the food supply and do not present any particular risk for humans (e.g. workplace exposure) or the environment" (EAC-vNHP, 2010).[18] That being said, Health Canada points out on its website that one should not take for granted that natural products are always safe (VDD, 2006a).

In 2010, the Committee published a report that included the following recommendations:

- to develop a "fast-track" process for products which are unlikely to affect the health of animals or humans and which will not compromise the safety of the food supply (i.e., low-risk or "presumed safe" products);
- to prioritize human and animal safety above other considerations in regulating vNHPs and to classify these products based on their potential risk to health;
- to develop and implement safety standards for all vNHPs to facilitate their market authorization, with higher-risk products being required to meet higher standards;
- to conduct pre-market reviews of products which cannot be presumed safe, and to invest in post-market surveillance of vNHPs; and
- to inspect companies' records and facilities, taking compliance and enforcement action as necessary (EAC-vNHP, 2010).

The Committee devoted much of its attention to developing specific recommendations around expediting marketing approval for "presumed safe" vNHPs. Canada has followed up on these recommendations by designing and implementing the Interim Notification Pilot Program for Low-Risk Veterinary Health Products (LRVHPs), which began operating in early 2012 (Health Canada, 2012b). This is a voluntary program for LRVHPs administered to dogs, cats, and horses not intended for food, which involves the approval of Notification Numbers for firms importing or manufacturing applicable products; while registered products do not formally have marketing authorization, Health Canada will typically not act to prevent the importation, manufacture, or sale of these products. The program is administered by a third party: North American Compendiums.

The stated purpose of this temporary program is to "assess the effectiveness of a streamlined approach to oversee LRVHPs with a view to informing the development of a new veterinary drugs framework," as well as to "educate the members of the industry on important issues such as quality controls and Good Manufacturing Practices," which are likely to figure into future regulatory measures aimed at LRVHPs (Health Canada, 2012b). A streamlined registration procedure for homeopathic veterinary medicinal products also appears to be in place in the EU for both companion and food-producing animals, provided, among other things, that these products are sold in sufficiently low concentrations and there is no specific indication on the label (ECHAMP, 2012).

In recent stakeholder consultations held to inform the development of a separate regulatory framework for veterinary drugs, Health Canada proposed a product registration model that would be applied to eligible veterinary drugs, based on the requirements of the Interim LRVHP (VDD, 2013c).

[18] The basis for the presumption of safety is not clear.

It is unclear if the existing Canadian program involves a post-market surveillance component, as recommend by the EAC-vNHP in 2010. Lack of post-market surveillance of vNHPs was identified by key informants as a weakness of Health Canada's current approach to veterinary pharmacovigilance, which is described in more detail in Section 4.3.

### 4.3.3 Pre-market activities and standard-setting

**The VDP has eliminated a considerable backlog of veterinary drug submissions and dramatically reduced the average time to decision. It also has introduced a variety of other initiatives to improve the efficiency of the review process, including parallel review with the US FDA for technical sections of companion animal submissions; a streamlined process for low-risk veterinary natural health products and generic submissions; a specialized approval process for minor use, minor species drugs; and increased information sharing with international counterparts.**

Over the evaluation period, as part of this activity, the VDP has emphasized the development of policies, processes, and tools to facilitate the submission review process, as well as the ongoing establishment of MRLs and the adoption of international standards. Pre-market activities and establishment of MRLs are discussed below, while adoption of international standards is described in Section 4.4.7.

#### Submission review

One of Health Canada's main pre-market activities under the VDP is reviewing veterinary drug submissions and giving market authorization to products deemed safe and effective. A central preoccupation for the VDD over the evaluation period, as for other directorates within HPFB, has been the timely review of product submissions, in a context of increased volume and complexity of submissions. The evaluation evidence suggests that the VDD has been successful in reducing the amount of time required for submission review over the evaluation period.

There are several types of veterinary drug submissions in Canada[19]:

- New Drug Submission (NDS)/Abbreviated New Drug Submission (ANDS). These involve approval for new and generic veterinary drugs, respectively.
- Drug Identification Number (DIN) submissions. This process applies to Division 1 drugs, i.e., drugs that have typically been on the market for many years and are not new drugs.
- Administrative NDS/ANDS. These pertain to changes in administrative information relating to the drug, such as the brand name.
- Supplemental NDS (SNDS)/Supplemental ANDS (SANDS). These are required in the case of significant manufacturing changes or modified conditions of use (labelling) for previously approved drugs.

[19] A submission typically consists of six distinct parts, including the Master Volume and sections devoted to manufacturing and quality control, animal safety, product efficacy, human safety, and environmental impact (VDD, 2007b). See Appendix C for the details.

- Notifiable Changes (NC). These are required in the case of minor manufacturing changes or changes to the adverse event profile or condictions of use.[20]
- Investigational New Drug Submissions (INDS)/Experimental Study Certificate Submissions (ESCS). Approval of an INDS enables manufacturers to supply a new drug to qualified investigators to assess its safety and efficacy, while issuance of an ESCS allows for manufacturers to sell to a qualified investigator an unapproved drug for the purpose of conducting studies in animals.
- Emergency Drug Release Submission (EDRS). An EDR may be issued to authorize the sale of a limited quantity of a drug not currently approved for sale in Canada to a veterinarian for emergency use.

Submission review is a complex process that begins with an initial screening phase to determine whether the submission has an acceptable format and sufficient supporting information. This is followed by a detailed review to assess animal safety and efficiency, human food safety (for food animal drugs), and quality of chemistry and manufacturing. If the submission is determined to be in compliance with the *Food and Drug Regulations*, VDD issues a Notice of Compliance (NOC) to the sponsor. A DIN is issued after issuance of an NOC.

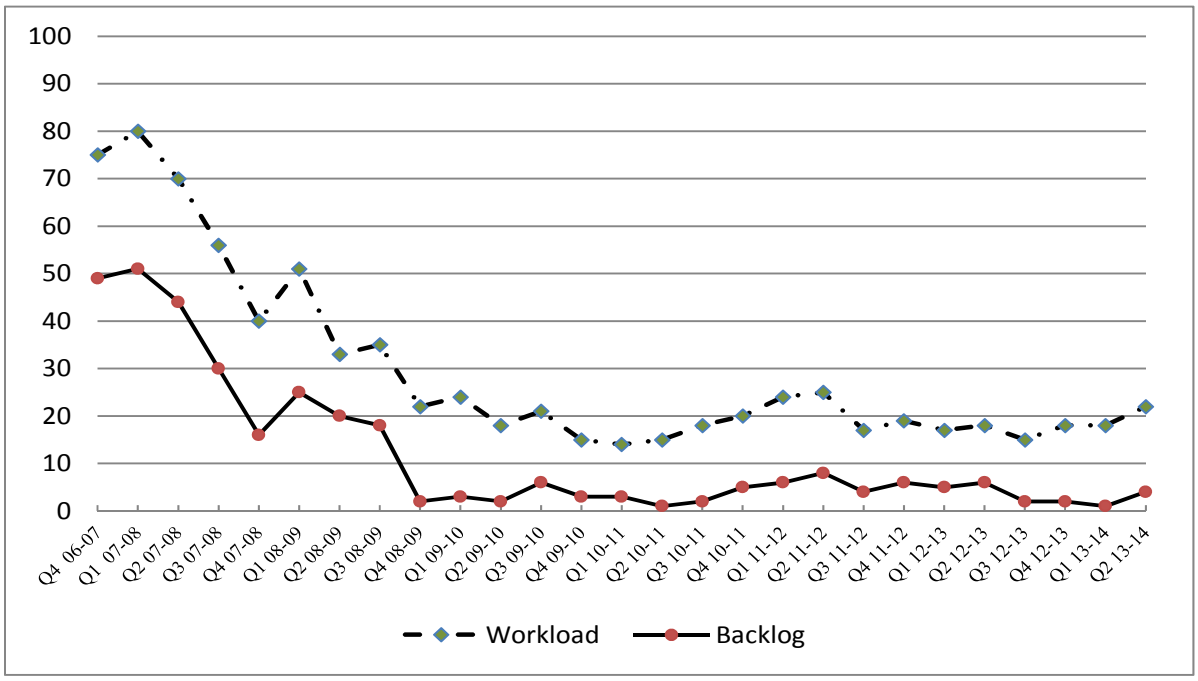
The VDD has implemented several initiatives to improve the efficiency of the review process. The VDD began implementing Management of Regulatory Submissions (MoRS) in July 2005 (Health Canada, 2005b), which was intended to expedite the processing of veterinary drug submissions and bring the VDD's activities in line with the *Treasury Board Policy on Service Standards for External Fees* (Boulay, 2005, p. 7).[21] The MoRS specifies targets in days for several classes of submissions; see Appendix B for the details.

The available data suggest that since the implementation of MoRS targets, the VDD has succeeded in eliminating a considerable backlog of new drug submissions, as well as drastically reducing the average time required to decide whether new drugs should be approved. As shown in Figure 1 below, there was a significant decline in workload and backlog associated with new drug submissions between Q4 FY 2006–07 and Q4 FY 2007–08, followed by a less rapid but still notable decline over FY 2008–09. Between Q4 FY 2008–09 and Q3 2010–11, workload remained stable at a relatively low level, while backlog was negligible.

[20] Notifiable Changes are not explicitly supported by regulation.

[21] Health Canada initially began charging user fees in 1994–95 for evaluation of new drugs, but the evaluation could not determine when such fees were introduced for review of veterinary drug submissions.

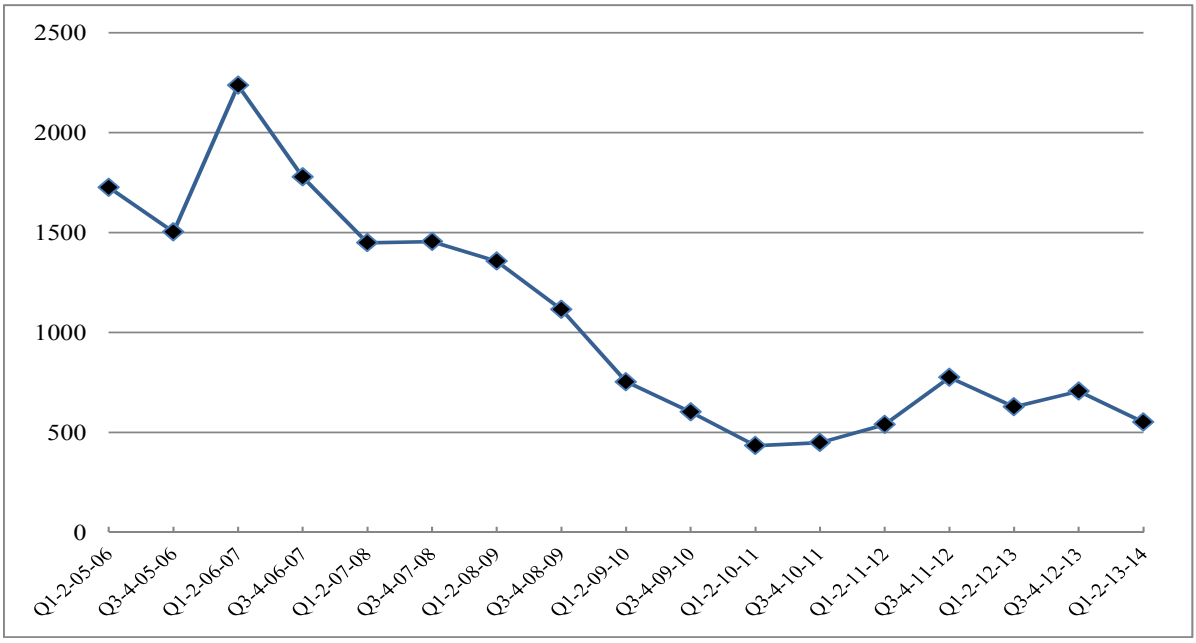
**Figure 1 – Workload and backlog for new drug submissions**
**Q4 FY 2006-07 to Q3 FY 2010-11**




Source: HPFB, 2011a

Similarly, the time required to complete the screening and review of new drug submissions has also declined in recent years. As shown in Figure 2 below, while average total time to decision for new drug submissions increased sharply between the last half of FY 2005–06 and the first half of FY 2006–07, it has declined almost continuously since that time. The average total time to decision in Q1–Q2 FY 2010–11 was 434 days, compared with 602 days in the last half of FY 2009–10 (HPFB, 2011a, p. 1), and well over 2,000 days in the first half of FY 2006–07. However, in 2011–12, the average total time to decision rose to 657 days, evidently as a result of a surge in submissions during the previous year, although the VDD was expected to meet its target of 600 days for submission review by March 2013 (AAFC, 2013).

**Figure 2 – Average time to total decision (days) for new drug submissions Q1 FY 2005-06 to Q1 FY 2010-11**




Source: HPFB, 2011a

As for the proportion of veterinary drug submissions meeting performance targets, the available performance reporting indicates that whereas MoRS targets were being met consistently in FY 2008–09, performance may have degraded somewhat in FY 2009–10 and 2010–11 (see Appendix B for detailed data). Contributing factors may include an increased number and complexity of submissions (HPFB, 2011b, p. 3) and resource constraints (HPFB, 2010c, p. 3), as well as a change in the way performance is evaluated.[22]

According to Health Canada's 2011–12 DPR, in FY 2011–12, 89% of regulatory decisions for pharmaceutical veterinary drugs were made within service standards (Health Canada, 2011f).

In addition to introducing service standards for submission review and tracking review performance, the VDD has also undertaken numerous other initiatives to improve the efficiency of the submission review process:

- developing and implementing various guidance documents for industry, including guidance on management of regulatory decisions, new drug submissions, generic drug submissions, dispute resolution, post-NOC changes relating to quality, safety and efficacy, and priority review of drug submissions, as well as, most recently, electronic submissions;

[22] Although performance was initially evaluated in terms of whether the average time to decision of all submissions being screened or reviewed was less than the target, by the end of FY 2010–11, the target had changed to whether 90% or more of submissions were being screened or reviewed within the target times.

- providing information to manufacturers, through issuing Update Notices for submissions exceeding the performance targets, and migrating all active submissions to HPFB's Drug Submission Tracking System (DSTS) to allow manufacturers to monitor the status of their submission during the review process;
- in response to attrition in its pre-market regulatory capacity in the mid-2000s (VDD, 2006b), establishing a partnership with the CVMA to generate a list of private sector veterinarians interested in contract review work (VDD, 2007c), and making arrangements to receive toxicology evaluation services from the HPFB's Food Directorate (HPFB, 2010a);
- piloting a project with the United States Food and Drug Administration's Centre for Veterinary Medicine (US FDA CVM) on parallel review of the technical sections of companion animal submissions, and announcing the first simultaneous approval of a veterinary drug application under the parallel review process on December 14, 2012[23] (GoC, 2012c);
- introducing the voluntary Interim Notification Pilot Program for LRVHPs in 2012;
- streamlining the review of generic drug submissions through publication of an internationally harmonized guidance in April 2010 (VDD, 2010a) and reducing the number of days required for the first and second review stages for generic drug submissions; some funding for these activities was provided through Growing Forward;
- introducing a specialized approval process for MUMS drugs; and
- collaborating with international counterparts to share information and increase the use of foreign data and/or reviews (see Section 4.7.7 for the details).

Recent VDD documentation indicates that Canada is now accepting new drug submissions in US format, with two submissions identified by early 2012 for parallel review (HPFB, 2011b, pp. 2, 6). The "US format" is a phased or rolling review process, in "which portions of a submission are received and reviewed by the agency as they are generated by the industry sponsor [which differs] from the current process where the information is provided to the agency in a full package when all the information has been generated by the industry sponsor" (HPFB, 2010c, p. 11).

Veterinary drugs are also included in Health Canada's Use of Foreign Reviews Pilot Project, which was launched in October 2011 and is set to run until March 2013.[24] The Foreign Reviews Pilot Project was Health Canada's response to the 2011 report of the Auditor General on regulating pharmaceutical drugs, which noted that Health Canada was not meeting its service standards for submission review and recommended, among other things, that the Department give due consideration to the use of foreign regulatory information in the review process (OAG, 2011, pp. 15–16).

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[23] According to the Government of Canada's announcement of the product approval, Health Canada and the FDA "worked collaboratively from the same fundamental effectiveness data set" to approve the drug (GoC, 2012c). The review was completed under an initiative of the Canada United States Regulatory Cooperation Council, which was created in February 2011 to "speed timely access to products while maintaining safety standards, and to eliminate duplications and differences in the regulatory arena that may limit timely access to products, slow trade and investment opportunities, and add costs to manufacturers and consumers" (GoC, 2012c).

[24] The pilot applies to human and veterinary biologics, disinfectants, radiopharmaceuticals, and pharmaceuticals (collectively referred to as "drugs"), as well as medical devices.

Finally, in stakeholder consultations held in early 2013, the VDD put forward for consultation a proposed model for veterinary drug applications that includes introducing a process "that would provide pathways to tailor the supporting information requirements to the specific circumstances of a drug" (VDD, 2013d, p. 1). More specifically, the VDD proposed two types of evidence pathways — full and alternative — where the latter would allow for "derogations" from the complete set of data requirements when, for example, there is a history of safe use of a product or approval by another trusted regulator (2013d, p. 4).

The 2011 IFAH survey found that the Canadian animal health products industry is pleased with improvements made by the VDD in recent years to the management of product submissions, including the introduction of performance standards, the shortened time for review, the reduced backlog, the streamlined approval process for low-risk products, and improved communications and cooperative relationships with both industry and foreign regulatory agencies (BioBridge Ltd, 2012, p. 3).

Among stakeholders participating in this evaluation, views were mixed regarding submission review. Although almost all respondents to the industry survey believe that Health Canada's pre-market activities are adequate to ensure the safety of veterinary drugs, only 3 of the 10 respondents agreed that reviews are timely (notwithstanding the substantial reductions in review time that have been achieved) and that Health Canada provides industry with timely information on whether reviews are meeting established service standards.

External key informants who could comment on submission review generally agreed that improvements have been made in the timeliness of the process. Suggestions for further efficiencies included more extensive use of electronic submissions and rolling/staggered submissions, acceptance of foreign data packages and use of foreign reviews, and more frequent joint reviews. A few external stakeholders expressed concern that recent Health Canada staffing/funding cuts may compromise the effectiveness and/or timeliness of the pre-market review process.

## Establishment of MRLs

One of the VDP's main standard-setting activities is the ongoing establishment of MRLs. As described in Section 4.1, in excessive concentrations, veterinary drug residues can adversely affect human health, and many jurisdictions, including Canada, have therefore taken steps to manage human exposure to these residues. A common tool in this regard is the MRL, which Canada defines as "an amount of residue that could remain in the tissue or food product derived from a food-producing animal that has been treated with a veterinary drug [which] is considered to pose no adverse health effects if ingested daily by humans over a lifetime" (VDD, 2003c).

An Administrative MRL (AMRL) is identical to an MRL (i.e., derived using the same scientific processes), except that the regulatory process to publish this information remains ongoing; that is, the residue limit has been identified but has not yet been incorporated into the *Food and Drug Regulations* (VDD, 2003c). The introduction of AMRLs in Canada was intended to address the long delays (up to two years) between the issuance of approval for new veterinary drugs and the promulgation of MRLs, which was described as "creating difficulties and costly delays for the producer [without] contributing to enhancing public health" (VDD, 2003d).

As of May 2012, the VDD had established 269 MRLs for 88 pharmacologically active substances, including 155 MRLs and 114 AMRLs (VDD, 2012). Establishment of some of these MRLs was undertaken using funding provided through the veterinary drugs component of Growing Forward, one of the objectives of which is greater harmonization of technical requirements, including MRLs, for veterinary drug approvals between the US and Canada (AAFC & Health Canada, 2009, p. 5).[25]

As such, under Growing Forward, the VDD identified a prioritized list of approved drug entities with US MRLs that required Canadian MRLs, targeting the establishment of three Canadian MRLs per year. To date, the VDD has established Canadian MRLs for 25 drug entities that have US MRLs, exceeding the target of three per year (AAFC, 2013). Also under Growing Forward, the VDD produced a draft comparison study in 2009 comparing the Canadian and US MRL processes, and an action plan was targeted for March 2010 (HPFB, 2010d). Neither the comparison study nor the action plan was available to the evaluation.

### 4.3.4 Post-market surveillance

**The VDP's post-market surveillance activities include monitoring of adverse drug reaction reports, signal detection, causality assessment, and post-market actions. Perceived shortcomings include under-reporting of adverse reactions by end-users, lack of adverse reporting requirements for unapproved imported products, and lack of surveillance of veterinary natural health products.**

Enhancing post-market surveillance, also known as pharmacovigilance, is one of the main themes of HPFB's regulatory modernization initiative. The VDP's activities in this area include ongoing collection and assessment of national and international post-market safety data and adverse drug reaction reports, and national and international cooperation relating to post-market surveillance. That being said, based on the evaluation evidence, it is unclear what specific enhancements to the post-market surveillance of veterinary drugs were planned and undertaken by Health Canada over the evaluation period.[26]

[25] Differences between MRLs in various jurisdictions may be attributable to the use of different methodologies, as well as to different risk tolerances.

[26] For unknown reasons, veterinary drugs are not included in three strategies under the Health Products component of the FCSAP, aimed at improving post-market surveillance, namely Strategy #2 (pharmacovigilance planning), Strategy #3 (risk management and mitigation strategy), and Strategy #7 (Periodic Safety Update Reports).

Health Canada's website defines pharmacovigilance in the context of veterinary drugs as "Adverse Drug Reaction (ADR) reporting or post-market surveillance to monitor the safety and efficacy of veterinary drugs" (VDD, 2004a). Under the *Food and Drug Regulations*, manufacturers are required to report to Health Canada within 15 days regarding any suspected adverse reactions occurring in Canada and any serious and unexpected ADRs occurring outside the country (GoC, 2012a, sec. C.01.017). Veterinarians and technicians are strongly encouraged — but not required — to report such reactions (VDD, 2011c). A recent amendment to the regulations requires manufacturers to notify Health Canada if the risk-benefit profile of a drug changes significantly; allows Health Canada to direct manufacturers to provide summary reports or case reports on a drug's safety and effectiveness; and requires manufacturers to maintain various documents related to safety and effectiveness for 25 years (GoC, 2012a, sec. C.01.018).

VDD key informants noted that over 98% of all reports received by the VDD occur in animals, although veterinary drug adverse reaction reporting encompasses reports of reactions occurring in both animals and humans.[27]

Within the VDD, the Pharmacovigilance Unit maintains a database of records of suspected adverse reactions, in accordance with the guidelines stipulated by the VICH (VDD, 2004a). VDD key informants reported that a shortcoming of the current database is its lack of signal detection capabilities; specific queries must be generated based on information obtained from other sources, such as the pre-market review, PSURs requested from manufacturers, or VDD's international counterparts. VDD key informants reported that the directorate is considering upgrading to a system with automated signal monitoring and detection capabilities, such as the systems used by industry and other international regulators.

VDD key informants reported that each domestic adverse reaction report receives a causality assessment, and based on "the number of reports, their similarity and the degree of reaction," the VDD may consider such steps as adding new warnings, contraindications, or human safety information to labels; recalling a particular lot of drug; or removing a drug from the market (VDD, 2004a). As appropriate, actions taken in response to post-market safety issues are undertaken in coordination with the Inspectorate (e.g., recalls).

Canada has adopted two VICH guidelines relating specifically to veterinary pharmacovigilance, namely *Management of Adverse Event Reports (AERs)* (GL 24) and *Management of Periodic Summary Update Reports* (GL 29) (VDD, 2011d). The VDD has also established agreements with regulatory counterparts in other jurisdictions, including arrangements for the exchange of pharmacovigilance information (Health Canada & European Medicines Agency, 2009; Health Canada, 2003b, 2006).

[27] Adverse reactions in humans could stem from accidental or other exposure to a veterinary drug, such as accidental self-injections in a feedlot context or accidental ingestion of a veterinary drug by a pet owner who has confused an animal medication for their own.

Among external key informants and survey respondents who participated in this evaluation, views were mixed on the adequacy of Health Canada's approach to ADR reporting and post-market surveillance activities relating to veterinary drugs. Areas of perceived weakness included the following:

- under-reporting of ADRs by end-users, including livestock producers and veterinarians;
- lack of awareness and understanding of Health Canada's ADR reporting requirements among foreign manufacturers;
- lack of ADR reporting requirements for unapproved imported products, including APIs;
- lack of attention to product efficacy in ADR reports, which key informants said is important in the context of AMR;
- lack of post-market surveillance of vNHPs; and
- inadequate resources for post-market surveillance of veterinary drugs.

In addition, some stakeholders have commented critically in the literature on the absence of publically available pharmacovigilance data in Canada related to veterinary drugs. For example, Woodward (2009) has observed that although Canada's veterinary pharmacovigilance program is, in many respects, similar to systems operating in other jurisdictions, unlike other jurisdictions, there is "surprisingly little" pharmacovigilance data publicly available in Canada (p. 147). Indeed, information on the number and types of veterinary drug adverse reactions is not publicly reported in Canada, unlike the US, Australia, and the EU (APVMA, 2012; Center for Veterinary Medicine, 2012b; CVMP, 2012). It is also noteworthy that both the EU and the US have electronic reporting of veterinary drug adverse reactions to encourage reporting and facilitate analysis, whereas Canada does not.

### 4.3.5 Compliance and enforcement

**Compliance and enforcement activities include education, consultation, and information; compliance monitoring through GMP inspections and inspections for compliance with MRLs; and voluntary and regulatory compliance and enforcement measures in response to non-compliances. The VDP's approach to GMP inspections for veterinary drugs is perceived as problematic by the animal health products industy, which considers it inappropriate to apply to veterinary drugs standards that are appropriate in the context of human drugs.**

As with post-market surveillance, although enhancing compliance and enforcement is one of the main themes of HPFB's regulatory modernization initiative and is presumably applicable to veterinary drugs, the evaluation did not find much evidence of plans for enhancements in this area specifically in relation to veterinary drugs. Rather, this activity has consisted of continuous and ongoing attendance to particular tasks by the Inspectorate, which it also carries out for other health products regulated by Health Canada.[28] However, some of the VDP's work in policy and regulatory development, particularly in relation to OUI and APIs, relates to compliance and enforcement.

[28] An overview of the Inspectorate's responsibilities with respect to veterinary drugs was given in Section 2.1.2.

One of the Inspectorate's main tasks is undertaking GMP inspections and issuing Drug Establishment Licenses (DELs). DELs are required for "any person in Canada engaged in any of the six licensable activities with respect to drugs in dosage form" (Inspectorate, 2012). The six licensable activities include fabrication, packaging/labelling, testing, importing, distributing, and wholesaling. To receive a DEL, an establishment must pass an inspection conducted by the Inspectorate, verifying compliance with Part C, Divisions 2 to 4 of the *Food and Drugs Regulations*, which relate to GMPs. This includes requirements for the premises, equipment, personnel, sanitation, raw material testing, manufacturing, quality control, packaging material testing, finished product testing, record keeping, sample retention, sterile product handling, and product stability (GoC, 2012a).

Thus, GMP inspections, through which the Inspectorate "assesses whether drugs are consistently produced and controlled in such a way as to meet the quality standards appropriate to their intended use, as required by the marketing authorization" (Inspectorate, 2007b, p. 6), form the basis of DELs. Domestic establishments subject to a GMP inspection are classified as compliant, non-compliant, or compliant with terms and conditions. [29] Inspections occur in cycles of 24 months for fabricators, packagers/labellers, and testing laboratories, and 36 months for importers, distributors, and wholesalers.

Health Canada's current approach to GMP inspections for veterinary drug establishments is perceived as problematic by many within the animal health products industry. For example, 30% of respondents to the 2011 IFAH survey reported problems relating to GMP inspections stemming from "inflexibility of Health Canada's GMP unit and the application of inappropriate guidelines emanating from a human health perspective, including some that are not applied in USA or Europe to animal health products" (BioBridge Ltd, 2012, p. 15). More broadly, the survey found that Canadian industry considers the influence of the regulatory framework for human health products as the most important factor having an adverse impact on the Canadian industry. Similar thoughts were echoed by industry key informants who participated in this evaluation.

In this context, it is important to note that Health Canada has taken steps to recognize the uniqueness of veterinary drugs in GMP inspections, including publishing specific guidance describing how GMP requirements may be applied differently in the case of veterinary drugs (HPFB, 2011c).[30] Health Canada key informants also reported that the current regulatory reform initiative includes a complete assessment of all regulatory activities currently in place, with a view to modernizing the framework in light of a risk-based approach and creating a separate regulatory framework for veterinary drugs. In recent stakeholder consultations to inform the development of a separate regulatory framework for veterinary drugs, Health Canada proposed that GMP requirements for veterinary drugs eligible under the proposed registration pathway would be introduced that would be similar to those prescribed in the *Natural Health Products Regulations* (VDD, 2013e). According to the consultation document, existing GMP requirements for veterinary drugs would not change.

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[29] HPFB has established Mutual Recognition Agreements (MRAs) on GMP compliance with a number of international jurisdictions. MRAs represent agreements between Health Canada and another country on the equivalence of their respective GMP compliance programmes.

[30] Originally published in 2003, the guidance was updated in 2011.

Although most external key informants could not comment on whether Health Canada's compliance and enforcement activities are adequate to ensure industry compliance with the regulatory framework for veterinary drugs, those representing industry expressed concerns. The main concern is what these key informants regard as the inappropriate application of human GMP standards to veterinary drugs — a concern that was also expressed by respondents to the IFAH survey, as noted above. Some industry key informants also expressed concerns about insufficient resources devoted to compliance and a lack of enforcement at the end-user level. While it was recognized that Health Canada does not have jurisdiction over the use of veterinary drugs by veterinarians and livestock producers, it was also pointed out that regulatory reform to address the OUI and API issues would go some way toward addressing concerns relating to the use of unapproved drugs by end-users.

Finally, although the CFIA is not being evaluated as part of the VDP evaluation, it is important to note that it has responsibility for monitoring compliance in relation to veterinary drugs through several programs. Inspectorate and CFIA compliance and enforcement data are presented in Section 4.3.3.

### 4.3.6 Communication and stakeholder engagement

**The VDD has made a concerted effort in the last few years to improve its communications to and consultations with stakeholders, and there is general agreement among stakeholders that communications and consultations have improved substantially.**

Under its regulatory modernization initiative, HPFB has pursued two broad or overarching objectives in relation to communications and stakeholder engagement, namely providing Canadians with more information on health products, including more timely and accessible information, and making the regulatory system more open to consumer and other stakeholder input and involvement. Over the evaluation period, the VDP has undertaken a number of communication and stakeholder engagement activities with these broad objectives in mind, including the following:

- Posting information for veterinary drug end-users and the general public on its website, including (but not necessarily limited to):
    - advisories and warnings relating to veterinary drugs;
    - factsheets, Q&As, and similar information pieces on topics such as AMR, MRLs, ELDU, OUI and compounding, prudent use of veterinary drugs in livestock feeds, hormonal growth promoters, and vNHPs; and
    - information on how and when to report ADRs.
- Posting information for industry on the veterinary drug application and review process, along with associated policies and guidance documents.

- Issuing Update Notices to manufacturers on submissions exceeding performance targets and allowing manufacturers to monitor the status of their submissions during the review process via the DSTS.
- Holding regular meetings and consultations with stakeholders, including meetings with CAHI, the VDD Stakeholder Committee, and the CAHPRAC (see Appendix C for more information), and providing information on its activities via communiqués to stakeholders.
- Establishing Advisory Committees, EACs, and EAPs to guide regulatory and policy development on a variety of issues (see Section 4.4.5 and Appendix C for details on these committees).
- Conducting public and stakeholder consultations on draft guidances, proposed policies, and proposed amendments to the *Food and Drug Regulations*, including consultations on:
    - proposed MRLs for Amprolium, Bacitracin, Cloxacillin, Dichlorvos, Erythromycin, Gamithromycin, Meloxicam, Novobiocin, Penicillin G, and Toltrazuril (VDD, 2011e);
    - draft policies/guidance documents related to AMR, ELDU, OUI, vNHP, MUMS, NDS, and others; and
    - adoption of particular VICH guidelines, proposed regulatory amendments, and a variety of other issues, such as a proposed aquaculture policy (VDD, 2007a) and draft definition of a vNHP (VDD, 2007d, 2008a, n.d.).

Many external key informants noted that the VDD appears to have made a concerted effort over the past few years to improve its communications to and consultations with stakeholders, and most of these said that these communications and consultations have substantially improved. This is discussed in more detail in Section 4.4.1.

## 4.4 Achievement of outcomes

This section presents the findings from the evaluation with respect to the evaluation questions on outcomes. Overall, as described in Section 3.4, while Health Canada has engaged in many activities that should, in theory, produce the expected outcomes, data to support a definitive conclusion regarding the extent to which expected outcomes have been achieved are relatively limited. For this reason, the evaluation findings pertaining to program outcomes should be considered as a baseline.

### 4.4.1 Awareness and understanding

**While Health Canada's communications and consultations activities have improved in the past several years, there are opportunities to further enhance communications and/or consultations with stakeholders, especially veterinary drug end-users such as veterinarians and livestock producers.**

In the short term, Health Canada's communication and stakeholder engagement activities are expected to produce increased awareness and understanding by external stakeholders of risks and benefits related to veterinary drugs, and increased awareness and understanding among industry

of the regulatory framework for veterinary drugs. While it is not possible, on the basis of the available information, to determine if awareness has increased, Health Canada's communications and consultations activities have clearly improved in the past several years. That being said, there are opportunities to further enhance communications and/or consultations with stakeholders, especially veterinary drug end-users.[31]

**Stakeholder views on Health Canada's communications and consultations**

Among external key informants who could comment on the subject, many observed that Health Canada's communications have improved greatly in recent years. Generally speaking, these key informants believe that Health Canada has been effective at communicating with industry and veterinarians, but less effective at reaching livestock producers, who may not view themselves as one of Health Canada's client groups. It was also suggested that Health Canada relies on veterinarians to communicate information to livestock producers, and that most veterinarians receive this information indirectly through the CVMA or provincial veterinary medical associations. Health Canada key informants acknowledged that some stakeholder groups may be getting information indirectly through their associations, but pointed out that this is an efficient means of information dissemination in a context of limited program resources.

Notwithstanding improvements in Health Canada's communications to stakeholders, external key informants noted that many stakeholders rely on sources other than Health Canada for information related to veterinary drugs, such as provincial governments, provincial veterinary medical associations, and drug companies. Echoing these points, although some respondents to the survey of end-users consider Health Canada to be their most important source of information about the safety and effectiveness of veterinary drugs, for most, other sources are more important. These sources include veterinarians, the scientific literature, and the Global Food Animal Residue Avoidance Database (gFARAD), which, among other services, estimates withdrawal times for ELDU (Dowling, Doucet, Fortier, & Clark, 2004). The Canadian version, CgFARAD, is widely acknowledged as an important resource for control of residues from veterinary drugs (CVMA, 2010; Prescott et al., 2012; Szkotnicki, 2008).

A few external key informants attributed the success of Health Canada's communications in recent years to the efforts that provincial veterinary medical associations and other organizations have made to pass Health Canada information on to their members. These stakeholders believe that Health Canada should increase its efforts to liaise with provincial regulatory authorities and veterinary medical associations to further improve information dissemination.

With respect to consultations, external key informants who could comment on the issue likewise believe that, over the past four or five years, Health Canada has increased its efforts to consult with stakeholders regarding policy and regulatory development. It was noted that Health Canada has established various multi-stakeholder expert advisory committees and meets regularly with CAHI and CAHPRAC. That being said, the following concerns were expressed about Health Canada's consultation process:

- lack of transparency regarding Health Canada's consideration of the feedback it receives through consultations;

[31] See Appendix C for detailed information from the industry and stakeholder surveys.

- lack of consultations regarding some decisions or holding consultations pro forma (i.e., after decisions have already been made);
- reluctance on the part of Health Canada to consult stakeholders on veterinary drug issues unless the issue has already been discussed in relation to human drugs;
- insufficient time to consider and comment on proposed policy and/or regulatory changes;
- consultation fatigue (i.e., requests for feedback can be overwhelming);
- lack of representation by veterinary drug end-users in some consultations, and lack of communication to end-users regarding the possibility of providing feedback; and
- the complexity of the consultation process, including via advisory committees, which can dissuade participation.

Key informants' suggestions for improving the consultation process include separating discussions of veterinary drug and human drug issues, as appropriate; engaging stakeholders earlier in the process; asking veterinary medical associations and other associations to circulate requests for feedback to their members and asking them for a response; organizing targeted consultations on specific issues via face-to-face meetings and recording decisions and actions; and providing updates on activities and decisions following consultations.

Likewise, results from the surveys of end-users and industry suggest mixed views of Health Canada's consultations over the past 10 years, with industry seemingly more satisfied with the process than end-users. The majority of industry survey respondents agree that Health Canada has consulted adequately with the veterinary drug industry and that the existing consultation mechanisms provide an effective means for the veterinary drug industry to express their concerns and interests to the Department, although fewer believe Health Canada has taken the concerns and interests of the veterinary drug industry into account in policy and regulatory development. Overall, however, these findings are consistent with the 2011 IFAH survey, which found that the Canadian animal health products industry generally felt that "in the past 5 years [Health Canada's] attitude toward positive and cooperative discussion and problem-solving has improved dramatically" (BioBridge Ltd, 2012, p. 3).

Almost all industry survey respondents agree that pre-submission meetings are an effective mechanism for ensuring that product submissions meet Health Canada's requirements, a sentiment that was echoed by most industry key informants. However, a few key informants said that these meetings typically involve a lengthy process that can cost sponsors thousands of dollars. As a result, as an alternative, some sponsors are now requesting annual "pipeline" meetings to inform Health Canada about ongoing product development activities and to address any emerging concerns.

In comparison to industry, a minority of respondents to the end-user survey agreed that Health Canada has consulted adequately with veterinary drug end-users, that the existing consultation mechanisms are an effective means for end-users to express their concerns and interests to the Department, and that Health Canada has taken the concerns and interests of end-users into account in policy and regulatory development.

**Impact of communications and consultations on end-user awareness and understanding**

As noted above, Health Canada's communications and consultations activities are expected to produce increased awareness and understanding among external stakeholders of the risks and benefits associated with veterinary drugs. At least half of end-users surveyed rated themselves as having a strong understanding of:

- risk management measures to address antimicrobial resistance associated with the use of antimicrobial agents in food-producing animals;
- potential human health risks of AMR related to use of antimicrobial agents in food-producing animals;
- Health Canada's Policy on ELDU; and
- prudent use of veterinary drugs in livestock feeds.

Areas where understanding appears to be weaker include potential human health risks associated with the use of hormonal growth promoters in food-producing animals, how and when to report an ADR, and potential human health risks of ELDU in food-producing animals.

Furthermore, while many end-users report being aware of risk and safety information produced by Health Canada, fewer have actually used this information. Most frequently, end-users have used the policy on ELDU and information on MRLs for food-producing animals, whereas only a few have used information on potential animal and human health risks related to the use of unapproved drugs and hormonal growth promoters. Nevertheless, those who have used information produced by Health Canada generally found it timely, accessible, understandable, of high quality, and useful. Overall, one third of end-users agreed that Health Canada has influenced their understanding of animal and human health risks.

The survey revealed some uncertainties among end-users with respect to ADR reporting, which is voluntary for this stakeholder group. While most end-users are aware of Health Canada's information on how and when to report an ADR, considerably fewer reported that they have used this information, and only 18 percent (3/21) have actually submitted an adverse reaction report to the VDD in the past. Less than half of end-users agreed that Health Canada has clearly outlined what information end-users are encouraged to report, identified where within the department end-users should submit ADR reports, and defined what ADRs end-users are encouraged to report.

External key informants who could comment on the subject had mixed views on the extent to which veterinarians and other end-users are reporting ADRs. While some believe there is a high awareness among veterinarians of the need to report, others said that there is general under-reporting by veterinarians, who key informants said are more likely to report adverse reactions to the drug manufacturer rather than Health Canada. External key informants identified several factors that may contribute to under-reporting by veterinarians, including:

- lack of understanding of what reactions should be reported and where the reports should be submitted;
- uncertainty over whether the observed reaction was due to the drug or other factors;
- unwillingness to report reactions associated with incorrect product administration; and
- a perception that adverse reaction data may result in unwarranted restrictions on product use.

External key informants believe that livestock producers are unlikely to report ADRs to Health Canada. They said that many producers are likely unaware of the need to report, and, if they are aware, they are more likely to inform their veterinarian than Health Canada. Unfortunately, due to sample limitations and a low response rate, the end-user survey could not substantiate or refute these observations. However, the general problem of under-reporting of ADRs by end-users has long been recognized by Health Canada as a challenge for all of the health products it regulates.

**Impact of communications and consultations on industry awareness and understanding**

For industry, Health Canada's communications activities are expected to produce increased awareness and understanding of the regulatory framework for veterinary drugs. The survey of industry indicates that while most respondents report having a strong understanding of Health Canada's submission requirements for veterinary drugs, fewer have a strong understanding of GMP, establishment licensing, and mandatory adverse reaction reporting requirements, and only one reported a strong understanding of Health Canada's compliance activities.

All industry respondents were aware of information made available by Health Canada relating to its requirements for product submissions, GMPs, establishment licensing, and mandatory adverse reaction reporting, and most had also used this information. With one exception, all industry respondents were also aware of information on the electronic submission process, although only three had used this information. Somewhat fewer were aware of and had used information on Health Canada's regulatory compliance activities. Overall, industry respondents consider the information produced by Health Canada to be timely, accessible, understandable, of high quality, and useful.

Although external key informants reported that drug manufacturers take Health Canada's ADR reporting requirements very seriously, have a clear understanding of these requirements, and adhere to them closely, the survey of industry revealed some uncertainty among industry respondents in this area. Almost all industry respondents agree that Health Canada has clearly outlined the time frame for mandatory ADR reporting, but fewer agree that Health Canada has clearly identified where in the department reports should be submitted and clearly outlined what information must be included, and half agree that Health Canada has clearly defined what ADRs must be reported. In the event of an ADR that had to be reported, about half of respondents said their firm could provide the required information and complete the report in the required time frame.

### 4.4.2 Safety and effectiveness of veterinary drugs

**While there clearly are processes in place that are designed to ensure that drugs that enter the market are safe and effective, there is no concrete evidence of improvements in the safety and efficacy of veterinary drugs in Canada over the evaluation period.**

In the short term, Health Canada's pre-market activities are expected to result in increased safety and effectiveness (or efficacy) of veterinary drugs on the Canadian market. While there are clearly processes in place that are designed to ensure that drugs that enter the market are safe and effective, there is no concrete evidence of improvements in the safety and efficacy of veterinary drugs in Canada over the evaluation period.

Increased safety and effectiveness (or efficacy) is expected to follow primarily from a rigorous review process. As was described in Section 4.3.3, the information requirements for pre-market reviews of new veterinary drugs are complex and detailed, and all respondents to the industry survey agreed that Health Canada's pre-market reviews of veterinary drug submissions are rigorous. Industry survey respondents also generally agreed that Health Canada has adequate pre-market processes in place to ensure both the safety and efficacy of veterinary drugs, although end-users were less likely to agree. External key informants who could comment on the submission review process generally agreed that Health Canada considers the appropriate type and quality of information in pre-market review. Their suggestions for improvements, such as more frequent use of foreign reviews or data and greater use of risk-based approaches, related primarily to increasing process efficiency.

Increased safety and efficacy are in fact closely linked in program and HPFB documentation to a more efficient approval process. Expediting the processing of veterinary drug submissions is expected to lead to improved access to new veterinary drugs, which are presumed to have desirable features that can improve the outcomes of veterinary pharmacotherapy. In the past few years, as was described in Section 4.3.3, the VDD has made substantial improvements in the efficiency and timeliness of submission review.[32]

While these improvements support the conclusion that *timely access* to new veterinary drugs has improved, it does not follow that safety and efficacy have also improved. Furthermore, it is not necessarily clear that *increasing* the safety and efficacy of veterinary drugs falls within Health Canada's mandate as it is currently defined, which, it could be argued, does not extend beyond ensuring that products that are approved for sale in Canada are safe and effective.

## 4.4.3. Industry compliance

**Industry compliance with MRLs and compliance with GMP requirements generally is high. However, a shift to combined reporting for veterinary and human drug inspections makes it difficult to discern clear trends in GMP compliance within the veterinary drugs industry in particular. As the regulator responsible for veterinary drugs, Health Canada should retain its ability to report separately on veterinary drug industry compliance. A greater focus on compliance outcomes in reporting would also contribute to greater understanding of industry compliance.**

[32] Only a minority of end-users believe that Health Canada has adequate pre-market processes in place to ensure timely access to veterinary drugs — notwithstanding that access is the one area in which, it could be argued, there is evidence of real improvement.

In the short term, Health Canada's activities are expected to lead to increased industry compliance with regulatory requirements relating to veterinary drugs. In two areas — compliance with MRLs and compliance with GMP requirements — there is some data to support the conclusion that industry compliance is generally high. However, there is no evidence of *increased* compliance with Health Canada's regulatory requirements.

For example, data from the CFIA's National Chemical Residues Monitoring Program (NCRMP) show that over a three-year period between 2005–06 and 2007–08, approximately 99% of samples tested (eggs, dairy, honey, and meat) were in compliance with MRLs (CFIA, 2006b, 2008a, 2011c).[33] However, data from the CFIA's other compliance monitoring programs demonstrate somewhat lower levels of compliance[34]:

- Between 1995–96 and 2006–07, through the Medicating Ingredients Guarantee Verification Program, the CFIA found compliance rates averaging 58% for on-farm mills and 78% for commercial mills; in other words, an average of 42% and 22%, respectively, of medicated feed samples tested over this period contained medicating ingredients in excess of their guaranteed concentrations (CFIA, n.d.-a).
- Between 1991–92 and 2006–07, through the Drug Residue Contamination Inspection Program, the CFIA found that approximately 20%, on average, of non-medicated feeds manufactured in commercial and on-farm feed mills contained unintentional drug residues (CFIA, n.d.-b). [35]

As the CFIA has noted, medications in excess of their intended concentrations may result in toxicity to livestock or unacceptable residues in animal products, while those that are below their intended levels may be ineffective for their intended purpose and contribute to the development of AMR (CFIA, n.d.-a). Similarly, unintentional contamination can result in unacceptable drug residues in foods (CFIA, n.d.-b).

There is some evidence that industry compliance with GMP requirements is generally high. Table 2 below shows the number and outcome of domestic GMP inspections undertaken by the Inspectorate between 2003–04 and 2010–11. It is difficult to discern trends in GMP compliance due to changes in reporting approach and some lack of clarity regarding the data presented in reports. However, it is possible to say that the majority of domestic veterinary drug establishments were determined to be compliant with GMP requirements between 2003–04 and 2006–07.

Health Canada key informants reported that generally speaking, the inspection compliance rating for pharmaceutical drug inspections (human and veterinary) has been in the realm of 90% to 95% over the years. They also reported that compliance within the veterinary drugs industry is

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33 These compliance figures are for veterinary drugs only, not for the NCRMP as a whole.

34 CFIA representatives indicated that all non-compliant results are evaluated with follow-up action taken consistent with the nature of the non-compliance. Where products pose unacceptable risk to animal health or production or may result in human health risk due to residues in foods, product recalls and other product control actions are implemented. In addition to compliance and enforcement actions on specific results, CFIA uses results of guarantee verification and residue contamination programs to identify program priorities and direct additional inspection and sampling activities.

35 See Appendix C for more detailed data from the CFIA's inspection programs.

similar to that of the human drugs industry. The shift to combined reporting for veterinary and human drug GMP inspections in 2007–08, however, has made it challenging to demonstrate the level of GMP compliance within the veterinary drugs industry in particular.

**Table 2: GMP inspections and compliance ratings, FY 2003–04 to 2010–11**

| Fiscal year | Number of inspections** | Number compliant | Number compliant with terms and conditions | Number non-compliant | Compliance rate (%)** |
|---|---|---|---|---|---|
| 2003–04 | 30 | 22 | N/A | 7 | 76% |
| 2004–05 | 40 | 37 | N/A | 3 | 93% |
| 2005–06 | 43 | 39 | 1 | 5 | 91% |
| 2006–07 | 40 | 34 | 7 | 3 | 85% |
| 2007–08 | N/A | N/A | N/A | N/A | N/A |
| 2008–09 | *21 | | ^20 | 1 | 95% |
| 2009–10 | *31 | N/A | N/A | N/A | N/A |
| 2010–11 | 27 | N/A | N/A | N/A | N/A |

* Starting in 2007–08, formal inspection data presented in reports include both human and veterinary drug inspections combined. As such, inspection data specific to veterinary drugs could not be obtained for all years.

^ The original report does not specify whether these establishments were compliant, or compliant with terms and conditions.

** For some fiscal years, there is lack of clarity in the reports on what the data includes. For example, the sum of compliant, non-compliant, and compliant with terms and conditions does not equal the total number of inspections for these years. The compliancy rate figures for FY 2003–04 to 2006–07 have therefore been drawn directly from the original reports rather than calculated from the available figures.

Sources: Inspectorate (2004, 2005b, 2006, 2007c, 2008, 2009b, 2010b, 2010c).Data for 2010–11 provided by Health Canada.

Health Canada's aggregated approach to compliance reporting is in contrast to the approach taken by the US FDA, which separates compliance reporting based on the center responsible for regulating various categories of product. Thus, the FDA reports compliance data separately for the Center for Veterinary Medicine (veterinary drugs), the Center for Drug Evaluation and Research (human drugs), the Center for Biologics Evaluation and Research (biologics), and so on (FDA, 2013). Furthermore, under the Good Manufacturing Practices Work Plan, an initiative of the Canada-United States Regulatory Cooperation Council (RCC), Health Canada and the FDA are aiming to "enhance collaboration on enforcement and compliance by increasing mutual reliance on each other's routine surveillance good manufacturing practices (GMP) inspection reports", ultimately adopting an "ongoing framework" which may include, among other elements, a "joint GMP database used as a common repository to foster standardized sharing of GMP inspection reports", "routine exchange of inspection reports/data in order to reduce duplicate inspections", and "initiation of joint inspections of selected establishments" (Regulatory Cooperation Council Personal Care Products and Pharmaceuticals Working Group, 2012). Achieving these objectives would seem to demand a common approach to compliance reporting.

The available compliance data for veterinary drugs also show that:

- Relatively few recalls of veterinary drugs have involved Type I hazards, the highest category assigned by Health Canada.[36] Data on veterinary drug recalls between 2003–04 and 2010–11 show that, of the 57 recorded recalls over this time period:
    - 8.7% involved Type I hazards, i.e., cases in which use of or exposure to the recalled product would have had a relatively high probability of resulting in serious adverse health consequences or death.
    - 43.8% were classified as Type II hazards, i.e., cases in which use of or exposure to the recalled product could have had temporary adverse health consequences or a remote chance of generating serious health effects.
    - 42.0% were classified as Type III hazards, i.e., cases in which adverse health consequences due to product use or exposure were unlikely.

- Between 2003–04 and 2006–07, there were only seven compliance measures (other than recalls) relating to veterinary drugs, all of which were voluntarily conducted by the regulated party. There were no recorded instances of enforcement actions by Health Canada, such as seizures or prosecutions.
- Under the Border Integrity Program, the CBSA refers shipments that may contain non-compliant health products to the Inspectorate for inspection and determination of admissibility. Although data are not available for 2007–08 and 2008–09, the data for 2004–05 to 2006–07, 2009–10, and 2010–11 show that in these years, the Inspectorate recommended between 17% and 43% of shipments for refusal. In 2009–10 and 2010–11, 3% (n=9) of inspected shipments were found to contain counterfeit products and were refused admissibility for that reason.

More detailed information on the number of compliance measures, recalls, and border recommendations can be found in Appendix C. However, these measures are weak indicators of industry compliance, since many factors could influence trends in these areas and it is challenging to account for all possible factors that may contribute. As a result, any observed trends can be interpreted as signifying either success or failure of Health Canada's regulatory approach. For example, an increase in the annual number of recalls over time could signify either more unsafe products on the market (i.e., decreased compliance) or greater awareness by industry of the obligation to remove unsafe products (i.e., increased compliance). For these reasons, the data on compliance measures, recalls, border recommendations, and similar indicators of Inspectorate activities or outputs should not be used as the basis for conclusions about compliance.

[36] Industry is responsible for initiating recalls but must inform Health Canada when recalls are initiated. Health Canada may also request industry to undertake recalls, although it does not currently have the power to require a recall.

### 4.4.4 Adoption of safe behaviours

**There is some evidence that unsafe practices, including the use of antimicrobial agents, own-use importation, and importation and direct use of active pharmaceutical ingredients, are taking place in Canadian agriculture, although the magnitude of the problem continues to be a matter of debate. The impact of the VDP on end-user behaviour is an area for future research.**

In the intermediate term, VDP activities are expected to lead to adoption of safe behaviours related to the use of veterinary drugs by external stakeholders. In the absence of data on the use of veterinary drugs, it is challenging to draw conclusions on the extent to which this outcome has been achieved. The limited evidence that is available is mixed.

The literature review found some evidence that unsafe practices are taking place in Canadian agriculture, particularly with respect to the use of antimicrobials. For example, a recent CIPARS surveillance bulletin report identified an emerging trend (>10% prevalence) in ciprofloxacin-resistant *Campylobacter* in retail chicken in British Columbia and Saskatchewan (CIPARS, 2011, p. 1). Ciprofloxacin is a fluoroquinolone antimicrobial, which is a Class I agent of very high importance to human medicine (PHAC, 2011, p. 92). According to the bulletin, these findings suggest extra-label use of enrofloxacin in broiler breeder flocks to treat *Salmonella* (CIPARS, 2011, p. 2).

Similarly, while CIPARS reports of data obtained from CAHI on the volume of antimicrobial agents distributed by its members in Canada[37] show large reductions between 2006 and 2008 in the use of fluoroquinolones (very high importance to human medicine), lincoasmides (high importance to human medicine), and tetracyclines (medium importance to human medicine), over the same period, there were large increases in the use of aminoglycosides (very high to high importance), as well as trimethoprim and sulfonamides (both high to medium importance) (PHAC, 2009, pp. 66–67, 2010, pp. 65–66, 2011, pp. 80–81).

There are numerous limitations associated with these data, including changes in the way in which individual antimicrobial agents are aggregated, the relatively short time frame for which data are available, and the fact that distribution cannot be equated with use (PHAC, 2011, p. 80). Perhaps most importantly, these data do not include own-use imports or active APIs used in compounding. CAHI estimates that about one third of veterinary drugs used in Canada are imported (Handa & Webster, 2009, p. 914). Similarly, Handa and Webster (2009) cite reports that large quantities of antimicrobial agents are being imported from overseas and may be used without veterinary supervision in some factory farms (pp. 915–916).

On the other hand, there is also evidence that unsafe use of antimicrobials in Canadian livestock production is relatively limited. For example, Gow and Waldner (2009) determined that drug use in a population of 203 western Canadian beef herds during calving season was primarily therapeutic and that relatively few animals were exposed to antimicrobial drug therapy. The most commonly used antimicrobial agents in these herds were antibiotics of medium importance to

[37] For use in food, sporting, and companion animals and fish.

human medicine, although limited extra-label use of fluoroquinolones and cephalosporins was also observed. Another study of antimicrobial use on 24 beef farms in Ontario determined that less than 1% of the antimicrobials used by study participants involved the use of agents classifed as being of highest importance to human medicine, while 78% used antibiotics classified as being of lowest importance to human medicine (Carson, Reid-Smith, Irwin, Martin, & McEwen, 2008, p. 115). In short, while it seems clear that some unsafe use of antimicrobials is taking place in Canadian livestock production, the extent to which this is occurring is a matter of some debate.

Stakeholders who participated in this evaluation held mixed views regarding the extent to which end-users have adopted safe behaviours as a result of Health Canada's activities. Some external key informants believe that veterinarians and livestock producers are using veterinary drugs more safely, noting that awareness of issues such as AMR and withdrawal times has increased; that some veterinarians are discussing appropriate use of antibiotics with their colleagues; and that livestock producers are implementing on-farm monitoring systems. It was also noted that industry associations are using the VDD's categorization of antimicrobial drugs to prepare guidance materials for veterinarians.

However, others believe that use of veterinary drugs has not changed and that unsafe practices continue to occur. As examples, external key informants cited OUI and direct use of APIs, as well as use of antimicrobial OTC products without veterinary oversight. Concerns were also raised about an emergent practice in some provinces known as "bundling," by which pharmaceutical companies sell "packages" of veterinary drug products to livestock producers at a discounted rate. It was suggested that this may result in veterinary drugs being used inappropriately or unnecessarily.[38]

End-users who were surveyed were similarly divided, with one third reporting that Health Canada's policies and risk communications have influenced the way in which they practise veterinary medicine and/or use veterinary drugs. The remainder were either neutral, disagreed, or did not know.

### 4.4.5 Use of scientific evidence and risk-benefit analysis

**Generally speaking, Health Canada appears to use scientific evidence and risk-benefit analysis on a regular basis to inform decision making. Recently the Department has begun to implement regulatory reforms to address own-use importation and the use of active pharmaceutical ingredients.**

[38] Similar concerns could arguably be raised in relation to loyalty programs being offered by some pharmaceutical manufacturers, which allow livestock producers to earn points on purchases that can be redeemed for rewards or cash-back rebates.

In the intermediate term, the VDP envisions an increase in the use of scientific evidence and risk-benefit analysis to inform Health Canada decision making. Generally speaking, Health Canada appears to use scientific evidence and risk-benefit analysis on a regular basis to inform decision making. Recently the Department has begun to implement regulatory reforms to address own-use importation and the use of active pharmaceutical ingredients.

The use of scientific evidence and risk-benefit analysis is formally integrated into Health Canada's decision-making process. The Health Canada Decision-Making Framework for Identifying, Assessing and Managing Health Risks sets out an approach to decision making in which risk analysis and management activities are central (Health Canada, 2001a). The framework is presumably used to guide the VDP decision-making process, although the evaluation could not assess the consistency with which it is applied in practice.

Health Canada has established a number of expert and scientific advisory groups to provide guidance on regulatory and policy development in various areas (for an overview of these groups and their activities, please see Appendix C). Based on membership lists, these groups include representation from individuals with extensive education and training pertinent to the topics under consideration, and are characterized by relatively balanced membership, including academics, representatives from the CVMA and CAHI, as well as from a variety of producer groups, consumer associations, and provincial and federal governments. The EAC-vNHP and OUI Task Force appear to have included less academic representation than the other groups (Health Canada, 2009; OUI Task Force, 2008).[39]

Health Canada has used the recommendations of several expert advisory groups to guide policy and regulatory development. For example:

- The EAC on Antimicrobial Resistance Risk Assessment provided guidance on the development of the antimicrobial risk categorization document.
- The EAC-vNHP developed a definition of veterinary natural health products, and its recommendations were used to develop the Interim Notification Pilot Program for LRVHPs.
- The recommendations of the ELDU advisory committee informed the development of the ELDU Policy.

However, there are some instances where Health Canada has not followed up, or not followed up fully, on recommendations made by expert/scientific advisory groups. For example, Health Canada has not yet fully responded to several of the 2002 recommendations of the Advisory Committee on Animal Uses of Antimicrobials and Impact on Resistance and Human Health, including making all antimicrobials used for disease treatment and control available by prescription only and changing policies on the use of antimicrobials for growth promotion. Furthermore, Health Canada has not stopped direct importation of antimicrobial APIs, nor has it stopped the importation of antimicrobials not evaluated and registered by Health Canada by

[39] Handa and Webster (2009) report concerns held by some individuals that the OUI Task Force did not include adequate representation from public health experts (p. 916), although in its final report, the Task Force states that "other groups were asked to attend but were unable to participate" (OUI Task Force, 2008).

addressing OUI. At a recent conference on antimicrobial stewardship, Health Canada was criticized for not yet having addressed OUI and APIs by both scientific and industry stakeholders (Prescott et al., 2012). As previously noted, Health Canada key informants reported that the Department is continuing to work on its response to AMR and that, due to their complexity, OUI and APIs will be addressed in a new regulatory framework for veterinary drugs (see Section 4.3.2).

As already noted, Health Canada's information requirements for pre-market review of new veterinary drugs appear to be complex and detailed, and include consideration of international post-market data. With the move to a more risk-based approach to regulation, Health Canada has begun to implement ways to streamline data requirements for lower-risk products (see the discussion in Section 4.3.3). With respect to post-market surveillance, Health Canada key informants reported that adverse drug reactions and safety signals are monitored and used to inform decision making.

The evaluation did not receive post-market surveillance data or information on actions taken by Health Canada in response to identified signals in response to its requests for such information. However, based on publicly available sources, several examples were found of decisions made by Health Canada in response to post-market safety data:

- After in-depth analysis of reports of adverse events in Canada suspected to have resulted from use of ProHeart®6, an approved injectable sustained-release heartworm prevention product for dogs, Health Canada recommended that the product manufacturer revise the label to reflect these safety concerns and notify veterinarians of these revisions (VDD, 2006c).
- After identifying human health risks associated with accidental self-exposure to the veterinary drug Micotil® (i.e., a macrolide veterinary antibiotic), the VDD collaborated with the manufacturer of the drug to issue changes to the product monograph, and also issued notices to both veterinarians and hospitals encouraging safe handling procedures and providing recommendations about managing cardiac reactions resulting from human exposure to the drug (Health Canada, 2003a, 2004a).

In addition, Health Canada representatives indicated that in 2005, the VDD included ELDU restrictions on all ceftiofur product labels after CIPARS reported AMR surveillance data showing increased resistance in salmonella isolated from retail chicken where presumably this drug was being used in an extra-label manner.

There are also numerous documented cases of HRAs developed by the VDD in response to specific potential human health risks.[40]

[40] Additional examples of HRAs completed in response to requests by the CFIA can be found in Appendix C. Although the Inspectorate may also request HRAs, the evaluation did not receive any examples of such requests or any examples of HRAs completed by the VDD in response to Inspectorate requests.

- A discussion of malachite green on the CFIA's website mentions that leucomalachite green, a metabolite of malachite green, is believed to be carcinogenic. An HRA conducted by Health Canada determined that the "potential risk to humans from eating fish with levels of malachite green and or leucomalachite green residues at 1ppb or lower is remote, even if fish with these levels are consumed every day, over a lifetime" (CFIA, 2006a).
- An FAQ with respect to the threat posed by chloramphenicol in honey imported from China reports that after routine testing for drug residues in honey detected traces of that substance, Health Canada provided results of an HRA advising that the honey posed a small but serious health risk. As a consequence, it was recommended that the detained products not be sold in Canada, that potentially affected products be recalled from the market, and that the potential health risk be communicated to consumers (VDD, 2004b).
- In response to a request from the CFIA for an HRA for cattle intended for slaughter that have been fed a mixture of medicating ingredients, some of which are not approved for cattle, the VDD noted in its completed HRA that there were many uncertainties related to the combination of various approved drugs at recommended and higher-than-recommended levels, as well as the presence of unapproved drugs in the cattle ration (VDD, 2007e). As a result, the risks to human health from consumption of these cattle could not be predicted. As a precaution, the VDD recommended that the exposed cattle should not be slaughtered for human consumption for 50 days.

About half of end-users and just over one third of industry respondents agreed that Health Canada's policies and regulations are based on best available scientific evidence and an appropriate analysis of risk.

### 4.4.6 Timely regulatory system response to identified risks

**While there is insufficient evidence to support general conclusions regarding the extent to which the VDP's response to identified risks is timely, there are a few examples of long-standing issues that Health Canada has not yet acted to address through policy and regulatory change.**

A timely regulatory system response to identified risks is expected to result from VDP activities in the intermediate term. While there is insufficient evidence to support general conclusions on this outcome, there are a few examples of long-standing issues that Health Canada has not acted to address through policy and regulatory change.

The most systematic approach to answering this question would be to examine the elapsed time between Health Canada's initial identification of specific risks and its policy or regulatory response. Although several examples of Health Canada's response to specific identified risks were described above (e.g., adverse health events in animals stemming from use of ProHeart®6, and presence of chloramphenicol residues in honey imported from China), there is insufficient information in the available documentation to determine how much time elapsed between risk identification and response. Even if this information were available for these cases, they would be examples only and not necessarily indicative of the overall timeliness of the VDP's response.

Analysis of the timeliness of Health Canada's response is also complicated by difficulties in pinpointing when risks were first identified and when the Department may be considered to have responded, and by the absence of performance standards against which Health Canada's response may be compared.[41] For these reasons, an assessment of the overall timeliness of Health Canada's response to risks cannot be made.

That being said, it is clear that Health Canada has not implemented regulatory changes to address two issues that have been acknowledged for at least the past decade to pose potential risks to human and animal health and the safety of the food supply; namely, the ongoing practices of importation of unapproved veterinary drugs for own use and direct use of APIs. As was explained in Section 4.3.2, this is evidently not due to any failure on the part of Health Canada to recognize these potential risks or attempt regulatory change, at least with respect to OUI. Thus, other factors may explain the lack of progress in this area. According to Health Canada key informants, OUI and APIs will be addressed in a new regulatory framework for veterinary drugs, which is currently out for public consultation.

A minority of respondents to the industry and end-user surveys believe Health Canada has responded in a timely fashion to identified risks over the past 10 years.

### 4.4.7 International harmonization

**The VDP has been working toward greater international harmonization and has made progress in some areas. However, there is no evidence to support conclusions about the impact of harmonization on human health or food safety.**

In the intermediate term, VDP activities are expected to produce increased international harmonization of regulatory requirements for veterinary drugs. Ultimately, increased harmonization is expected to contribute to improved health of Canadians and increased safety of the food supply. The evaluation found evidence that the VDP has been working toward greater international harmonization and has made progress in some areas. However, there is no evidence to support conclusions about the impact of harmonization on human health or food safety.

Health Canada's Therapeutic Products Directorate (TPD), which plays an analogous role to the VDD with respect to pharmaceutical drugs and medical devices for use in humans, defines harmonization as "the development, adoption, and implementation of international technical standards for the development, registration, and control of pharmaceuticals and medical devices," as well as "the convergence of regulatory practices and processes" (TPD, 2004, p. 9). With this definition in mind, some of the VDP's international harmonization activities include the following:

- participating in the International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products (VICH) through participation in a variety of VICH meetings and working groups, and adopting 37 VICH standards to date (Health Canada, 2003c).

[41] It is unclear, for example, whether the VDP has established performance standards for its post-market activities. Some such standards have been developed by the Marketed Health Products Directorate for application to post-market activities related to human drugs and biologics, and others are in development.

- participating in the Codex Alimentarius Commission, which "develops harmonised international food standards, guidelines and codes of practice to protect the health of the consumers and ensure fair trade practices in the food trade" (Codex Alimentarius Commission, 2012) — the VDD's contributions to Codex Alimentarius include:
  - participating in meetings of the Codex Committee on Residues of Veterinary Drugs in Food (CCRVDF) and the Codex Intergovernmental Task Force on Antimicrobial Resistance;
  - drafting Canadian positions for the CCRVDF and leading an electronic working group of the CCRVDF on extrapolation of MRLs in species and tissues; and
- leading the Canadian delegation's contributions toward the Codex Intergovernmental Task Force on AMR, which created and revised Codex Guidelines for Risk Analysis of Foodborne Antimicrobial Resistance.
- signing MOUs and similar agreements on information sharing and regulatory cooperation with veterinary drug regulatory agencies in other jurisdictions, including Australia, Switzerland, New Zealand, the United Kingdom, and France; branch-wide MOUs on information sharing are also in place with both the US FDA and the European Medicines Agency for therapeutic products in general.
- establishing MOUs with various international agencies and organizations to undertake research activities, including Germany's Friedrich-Loeffler Institute and Institute of Novel and Emerging Infectious Diseases, and Australia's Prion Research Group.
- piloting a project with the US FDA on parallel review of the technical sections of companion animal submissions, and announcing the first simultaneous approval of a veterinary drug application under the parallel review process on December 14, 2012.
- working toward establishing a priority list of MUMS drugs for small ruminants approved in Australia and US, and developing protocols to share review reports on such drugs already reviewed in those jurisdictions.
- participating in international initiatives such as the Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme and Official Medicines Control Laboratories (OMCL) meetings and proficiency tests.

Regulatory harmonization initiatives such as these may have the potential to contribute to improved human health and safety of the food supply, but in the absence of any concrete evidence, the health and safety benefits of harmonization are more theoretical than real. In this context, it is noteworthy that the Action Plan for Canada's most recent regulatory harmonization initiative, the RCC — under which Health Canada and the US FDA recently completed the first parallel review of a veterinary drug — does not explicitly claim that RCC initiatives involving health products will promote public health. Instead, the Action Plan promises that these initiatives will "reduce unnecessary duplicative costs for manufacturers…further streamline regulatory decision making, and minimize the delays in bringing health and personal care products to the marketplace, thereby expanding consumer choice without compromising the safety, efficacy and quality of products" (GoC, 2011, p. 22).

### 4.4.8 Long-term outcomes

**It seems reasonable to assume that VDP activities have contributed to reducing health risks and adverse events associated with the use of veterinary drugs, to increased safety of the food supply, and to increased public confidence in veterinary drugs, the related regulatory system, and the food supply.**

In the long term, VDP activities are expected to contribute to reduced health risks and adverse events associated with the use of veterinary drugs, increased safety of Canada's food supply, and increased public confidence in veterinary drugs, the related regulatory system, and the food supply. It seems reasonable to assume that VDP activities have had an impact in these areas, although it is important to realize that many other factors may also influence these outcomes.

VDP activities such as timely approval of safe and efficacious drugs, prohibitions on the sale of certain products for use in food-producing animals for which no residue level is considered safe, management of drug residues in food, initiatives to influence the use of antimicrobial agents in food-producing animals, and post-market surveillance and compliance activities should, in theory, contribute to the safety of the food supply and reduced health risks. For example, the prohibition on the use of certain substances in food-producing animals has certainly averted adverse health effects in humans that would have occurred had the prohibition not been in place.

That being said, there are a number of policy and regulatory gaps which, if addressed, would further contribute to risk reduction and food safety. Most notably, direct use of APIs and importation of unapproved drugs for own use may pose more significant risks to human health and food safety than the risks associated with licensed veterinary drugs. Recently, Health Canada has started the process to address OUI and the importation and direct use of APIs by holding stakeholder consultations on a proposed regulatory approach to OUI and APIs.

As for public confidence, several recent public opinion surveys suggest that Canadians are quite confident in Canada's food safety system, with approximately nine in ten respondents reporting moderate or high levels of confidence in the system (CRA, 2012; Decima Research, 2010, pp. 19–20; EKOS Research Associates Inc., 2010, p. 3; Léger Marketing, 2011, p. 15). This compares favourably with focus groups conducted in late 2007, in which participants' confidence in the food supply was described as "moderate and precarious" (Les Etudes de Marché Créatec, 2007, p. 2), and a summary of recent public opinion research on the CFIA website suggests consumer confidence has been gradually increasing over the last few years (CFIA, 2011d). This research suggests that Canadians generally approve of Canadian standards and regulations in the area of food safety, and also that confidence in the Government of Canada may contribute significantly to their confidence in the food safety system itself.

Ultimately, Health Canada hopes to achieve a sustainable, cost-efficient, responsive and science-based regulatory system for veterinary drugs in Canada. Limited financial and human resource information makes it difficult to draw conclusions regarding the sustainability and cost-efficiency of the system, although indications are that the VDP has improved operational efficiencies in recent years and is undertaking various other initiatives that are intended to produce further improvements in efficiency (see Section 4.5 for a more detailed discussion). As

for the responsiveness and scientific basis of the regulatory system, Health Canada has made clear progress in addressing emerging issues and challenges over the evaluation period, and appears to base many of its policy and regulatory decisions in scientific evidence and risk-based analysis. On the other hand, there is room for improvements on some longer-standing issues (e.g. OUI and API).

### 4.4.9 Unintended consequences

**The evaluation identified few unintended consequences. However, unapproved veterinary drugs are being used in Canada as a result of own-use importation and the importation and direct use of active pharmaceutical ingredients.**

The evaluation identified relatively few unintended consequences of Health Canada's regulatory activities in relation to veterinary drugs. Perhaps most importantly, unapproved products are evidently being used in Canada as a result of OUI and the importation and direct use of APIs. Some key informants attributed the prevalence of these practices to longer drug submission review times, lower availability, and higher costs of veterinary drugs in Canada compared to other jurisdictions, and suggested that addressing these issues would help to reduce the frequency with which unapproved products are used.[42] However, as already noted elsewhere in this report, there is also widespread support for regulatory changes that would address OUI and prohibit direct use of APIs.

## 4.5 Efficiency and economy

**Changes in HPFB's approach to financial reporting over the evaluation period make it challenging to compare and analyze this information over time, and the available financial and human resource information is insufficient to support an analysis of efficiency and economy. The recent inclusion of veterinary drugs within financial reporting on the larger Pharmaceutical Drugs Program will complicate analysis of efficiency and economy in future, and may also hamper HPFB's ability to understand resource allocation and use for both programs.**

Changes in HPFB's approach to financial reporting over the evaluation period make it challenging to compare and analyze this information over time. Furthermore, as described below, the available financial and human resource information is insufficient to support an analysis of efficiency and economy. As a result, the evaluation could not assess the extent to which program resources were used as planned, whether program outputs were produced efficiently, or whether expected outcomes were produced economically.

For fiscal year 2007–08 and earlier, financial reporting was based on Health Canada's former PAA. Under this PAA, veterinary drug activities fell under the Health Products and Food Program Activity. Program sub-Activities were as follows:

- pre-market regulatory evaluation and process improvement.

[42] It should be noted that the price of drugs is outside of Health Canada's area of jurisdiction.

- information, education, and outreach on health products, food, and nutrition.
- monitoring safety and therapeutic effectiveness and risk management.
- transparency, public accountability, and stakeholder relationships.

Under this PAA, financial reporting was linked to these four Program sub-Activities and to sub-sub-Activities representing, at a more detailed level, the functional activities carried out by Health Canada personnel as part of the sub-Activities. However, it is not possible to link this information to what, since 2008–09, has been considered the VDP.

In 2007–08, Health Canada's PAA was restructured. Under the new PAA, the relevant Program Activity is Health Products, and the Program sub-Activities are as follows:

- Pharmaceutical Human Drugs
- Biologics and Radiopharmaceuticals
- Medical Devices
- Veterinary Drugs

Financial reporting was linked to these four Program sub-Activities from 2008–09 through 2010–11. However, in 2008–09, most HPFB Internal Services were allocated to the VDP, and in the latter year, Health Canada did not report financial information separately for the VDP. Rather, veterinary drugs-related activities were subsumed within the larger Pharmaceutical Drugs Program, which also includes human drugs. Subsequently, corresponding changes to the program governance structure were implemented in 2012–13 (as described in Section 4.2). Starting in 2011-12, a new PAA structure eliminated the Veterinary Drugs activities as a Program sub-Activity. The Veterinary Drugs Program activities are parsed under two PAA Program sub-Activities, i.e. Pharmaceutical Drugs and Food Safety and Nutrition.

As a result of these changes, it is challenging to develop an accurate financial picture of what is now considered part of the VDP over the entire evaluation period. For this reason, Table 3 shows total VDP expenditures for a limited two-year period from 2009–10 to 2010–11. In 2011–12, total expenditures were not reported for the VDP. Rather, VDD expenditures were reported and it was unclear what proportion of these expenditures related specifically to the VDP. Moreover, information on the expenditures of other VDP partners (the Inspectorate, RAPB, RMOD) was not available.

Based on more recent financial information provided by HPFB (2013–2014), HPFB has a limited ability to separate financial reporting for the VDD's food safety-related activities from its veterinary drug-related activities (limited to salaries and wages and miscellaneous operating expenses). However, information on the veterinary drug-related expenditures of the other VDP partners (such as the Inspectorate, RAPB, and RMOD) was not provided. Without this information, HPFB does not have a complete or accurate picture of the total costs of the VDP.

**Table 3: Total expenditures ($), VDP, 2009–10 to 2010–11**

| Directorate | 2009–10 | | | 2010–11 | | |
|---|---|---|---|---|---|---|
| | w/o revenue | w/ revenue | Revenue | w/o revenue | w/ revenue | Revenue |
| Veterinary Drugs | 7,702,792 | 7,162,488 | 540,304 | 6,735,700 | 6,084,826 | 650,874 |
| Therapeutic Products | 4,080 | 4,080 | 0 | 4,030 | 4,030 | 0 |
| HPFB Inspectorate | 24,298 | 24,298 | 0 | 3,511 | 3,511 | 0 |
| Marketed Health Products | 3,870 | 3,870 | 0 | 24 | 24 | 0 |
| Assistant Deputy Minister | 726,000 | 726,000 | 0 | 840,000 | 840,000 | 0 |
| Biologics and Genetic Therapies | 0 | 0 | 0 | 0 | 0 | 0 |
| Food | 0 | 0 | 0 | 0 | 0 | 0 |
| Health Products and Food Litigation Secretariat | 0 | 0 | 0 | 0 | 0 | 0 |
| Natural Health Products | 0 | 0 | 0 | 0 | 0 | 0 |
| Office of Nutrition Policy and Programs | 0 | 0 | 0 | 0 | 0 | 0 |
| Office of Consumer and Public Involvement | 0 | 0 | 0 | 0 | 0 | 0 |
| Policy, Planning and International Affiars | 0 | 0 | 0 | 0 | 0 | 0 |
| HPFB Obligations Fund | 0 | 0 | 0 | 0 | 0 | 0 |
| British Columbia, Alberta, Nunavut, Northwest Territories region | 315 | 315 | 0 | 0 | 0 | 0 |
| Ontario region | 2,574 | 2,574 | 0 | 57,223 | 57,223 | 0 |
| Quebec region | 308 | 308 | 0 | 0 | 0 | 0 |
| Atlantic region | 0 | 0 | 0 | 0 | 0 | 0 |
| Manitoba and Saskatchewan region | 0 | 0 | 0 | 0 | 0 | 0 |
| **Total VDP** | **8,464,236** | **7,923,932** | **540,304** | **7,640,488** | **6,989,614** | **650,874** |

Notes:
1. Figures do not include RAPB. Figures include Employee Benefit Plans (EBP).
2. Since overhead is not coded at the sub-program level, total VDP expenditures do not include overhead.

Source: HPFB.

Since the majority of VDP spending is allocated to the VDD,[43] it was thought that VDD expenditures in 2011–12 could be used to estimate the size of the VDP in that year. The results of this analysis are presented in Table 4. The figures would seem to indicate that VDD spending was $1.3 million (including revenues) in 2011–12, which is a substantial decline in comparison to the previous fiscal year, when VDD expenditures (including revenues) were approximately $6.1 million. The explanation for this discrepancy is unclear, but again, may indicate either an error or a major change in HPFB's approach to financial reporting. It is notable, however, that despite some fluctuations from year to year, revenues to the VDD declined between 2009–10 and 2011–12.

In short, the available financial information does not provide an accurate picture of total VDP expenditures over time.

Similarly, limited information is available on VDP budgets. For example, in 2010–11 and 2011–12, financial reporting at the Program sub-Activity level did not include budgeted amounts. Instead, budgeted amounts were only reported at the Program level (i.e., Health Products and

[43] With the exception of the 2008–09 fiscal year.

Food Safety and Nutrition).[44] This, combined with the changes in approach to reporting on expenditures described above, has made it challenging to compare budgeted amounts against actual expenditures for the VDP over time.

According to HPFB Financial Services, as of 2013–14 budgets will be coded at the PAA sub-Program level as well as at the Program level. However, given recent changes to HPFB's governance structure, reporting on both budgeted and actual expenditures for veterinary drugs presumably will continue to be included in financial reporting on the larger Pharmaceutical Drugs Program. While, as already noted, HPFB has a limited ability to isolate the costs associated with the veterinary drugs-related activities of the VDD from both its pharmaceutical and food safety-related activities, it is important to note that the VDP does not only consist of the activities of the VDD. It is not clear that HPFB's current approach to financial reporting enables it to produce a complete and accurate picture of the total cost of the VDP.

**Table 4: Total expenditures ($), VDD, 2009–10 to 2011–12**

| Program | 2009–10 | | | 2010–11 | | | 2011-2012 | | |
|---|---|---|---|---|---|---|---|---|---|
| | w/o revenue | w/ revenue | Revenue | w/o revenue | w/ revenue | Revenue | w/o revenue | w revenue | Revenue |
| Veterinary Drugs | 7,702,792 | 7,162,488 | 540,304 | 6,735,700 | 6,084,826 | 650,874 | 0 | 0 | 0 |
| Medical Devices | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Biologics & Radiopharmaceuticals | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Pharmaceuticals | 0 | 0 | 0 | 0 | 0 | 0 | 1,978,833 | 1,340,146 | 638,687 |
| **Sub-total Health Products** | **7,702,792** | **7,162,488** | **540,304** | **6,735,700** | **6,084,826** | **650,874** | **1,978,833** | **1,340,146** | **638,687** |
| *Overhead Health Products* | *1,107,193* | *1,107,193* | *0* | *989,325* | *989,325* | *0* | *1,064* | *1,064* | *0* |
| **Total Health Products** | **8,809,985** | **8,269,681** | **540,304** | **7,725,024** | **7,074,150** | **650,874** | **1,979,897** | **1,341,210** | **638,687** |
| Food Safety & Nutrition | 0 | 0 | 0 | 73,333 | 73,333 | 0 | 4,889,859 | 4,889,834 | 25 |
| **Total Health Products and Food Safety & Nutrition** | **8,809,985** | **8,269,681** | **540,304** | **7,798,358** | **7,147,484** | **650,874** | **6,869,756** | **6,231,044** | **638,712** |

Notes: Figures do not include RAPB. Figures include EBP.
Source: HPFB.

A number of other shortcomings in the data also limit their usefulness for analyzing efficiency and economy. For example, information on the number of full-time equivalents (FTEs) allocated to the VDP over the evaluation period is not available. While the available information shows that between 2000 and 2008, the number of FTEs within the VDD increased from 16.52 to 70.38, it is unknown what proportion of these FTEs were allocated to the VDP. Furthermore, there is no information on the number of FTEs allocated to the VDP within the other HPFB directorates (such as the Inspectorate). More recent information was not provided.

[44] That being said, according to the March 2012 HPFB Newsletter, the Veterinary Drugs Directorat's forecasted year-end budget for 2011–12 was $7.7 million, with forecasted expenditures of $6.86 million. This budget does not include funding for other Program activities that the other Program partners (e.g. the Inspectorate, RAPB, and RMOD) perform.

Perhaps more importantly, reporting by functional activities, which took place under the previous PAA, has not taken place since 2008–09. Some examples of functional activities (also referred to as Functional Areas) include screening, product assessment, new submissions, monitoring and surveillance, and education and outreach. Such reporting is important in analyzing efficiency and economy because it reflects the time spent by program staff performing various tasks or activities. As such, this information is important in assessing:

- allocative efficiency, which focuses on the relationship between resources and outcomes;
- operational efficiency, which focuses on the relationship between resources and outputs; and
- economy, which focuses on the optimization (including the minimization) of the use of resources.

In short, due to significant data limitations, the evaluation could not assess the extent to which program resources were used as planned, whether program outputs were produced efficiently, or whether expected outcomes were produced economically. That being said, there is evidence of improved operational efficiencies in recent years. As described in Section 4.3.3, the VDP has succeeded in eliminating a considerable backlog of new drug submissions in recent years, as well as drastically reducing the average time required to decide whether new drugs should be approved. The program also has undertaken various other initiatives to improve the efficiency of the pre-market review process, including introducing a specialized approval process for MUMS drugs and a voluntary Interim Notification Pilot Project for LRVHPs; streamlining the review of generic drug submissions; and piloting a project with the US FDA on parallel review. Since many of these changes have been quite recent, their impact on program efficiency and economy has not yet been determined. Furthermore, without the ability to clearly link financial and human resources to these activities, it will not be possible to determine their impact in these areas.

More extensive use of electronic submissions, acceptance of rolling submissions, acceptance of foreign data packages, and use of foreign reviews have the potential to introduce further efficiencies.

# 5. Conclusions and recommendations

This section of the report summarizes the main findings from the evaluation, draws conclusions, and makes recommendations.

## Relevance

The potential human health implications of veterinary drug use in food-producing and companion animals, stemming from the potential presence of veterinary drug residues in food, the risks associated with development of AMR, and direct exposure to veterinary drugs, suggest an ongoing need for Health Canada to regulate these products in order to protect the health of Canadians. Such a role is consistent with federal and Health Canada roles and responsibilities, as described in federal statutes and regulations, and aligns directly with Health Canada's strategic

outcome to inform and protect Canadians from health risks associated with food, products, substances, and environments. VDP activities are also well-aligned with federal priorities to strengthen food and consumer safety, as expressed in recent Speeches from the Throne, the FCSAP, and the Growing Forward Agreement. As part of HPFB's regulatory modernization initiative, the VDP is currently developing a new regulatory framework for veterinary drugs.

## Performance – program implementation

Regulatory authority for veterinary drugs in Canada is a shared jurisdiction of Health Canada, the CFIA, and the provinces and territories, with Health Canada and the CFIA responsible for carrying out pre- and post-market activities that are considered to be part of the VDP. Over the evaluation period, there has been no overall formal governance structure or coordinating mechanism for the VDP or the Health Canada component. However, Health Canada has a variety of formal and informal mechanisms and structures in place with its partners (e.g., Memoranda of Understanding, working groups and committees, etc.) to govern various aspects of the program.

On the whole, the existing approach to program governance appears to be working reasonably well. However, there may be some merit in revising and streamlining the existing logic model and performance measurement framework for the VDP to ensure that expected outcomes are fully consistent with Health Canada's mandate, Branch-level frameworks and tools, and the objectives of regulatory modernization. The logic model and framework could build on those developed for evaluation purposes and could be used on an ongoing basis as a program management tool. In spite of recent changes to HPFB's governance structure, under which veterinary drugs have been conceptualized as part of the larger Pharmaceutical Drugs Program, it is important from both an evaluation and a program management perspective that Health Canada retain its ability to report on both the outputs and the outcomes achieved of its regulatory activities related to veterinary drugs.

## Recommendation 1

**Health Canada should develop and strengthen its ability to report on the results of its regulatory activities related to the VDP.**

Health Canada has made considerable progress over the evaluation period in implementing its planned activities and, in the process, has responded to several emergent issues and challenges. One of its most notable accomplishments has been its success in eliminating a considerable backlog of veterinary drug submissions and dramatically reducing the average time to decision. The most recent available data indicate that in 2011–12, 89% of regulatory decisions for pharmaceutical veterinary drugs — compared to a performance target of 90% of decisions — were made within service standards. Health Canada has also undertaken several other initiatives to improve the efficiency of the review process, including launching a pilot project with the US FDA on parallel review of the technical sections of companion animal submissions; introducing a voluntary Interim Notification Pilot Program for LRVHPs; streamlining the review of generic drug submissions; introducing a specialized approval process for MUMS drugs; and increasing information-sharing with international counterparts, including exploring ways to increase the use of foreign reviews and data.

With respect to communications and consultations with stakeholders, external key informants noted that the VDD has made a concerted effort, particularly in the last few years, to improve its communications to and consultations with stakeholders, and they generally believe that these communications and consultations have improved substantially. That being said, there is some evidence that while Health Canada has been particularly effective at communicating with industry, and somewhat effective at communicating with veterinarians, it has not been effective at reaching livestock producers. Given the implications of veterinary drug use for human health and food safety, it is important that livestock producers understand the risks associated with the use of these products. A communication strategy could be implemented using intermediaries such as provincial veterinary associations and livestock producers to ensure Health Canada's risk communications are reaching veterinary drug end-users.

In the area of regulatory and policy development, although Health Canada has introduced a number of initiatives to address the complex problem of AMR, it has not yet fully implemented all of the 2002 recommendations of the Advisory Committee on Animal Uses of Antimicrobials and Impact on Resistance and Human Health. Its approach to date is also inconsistent with the 2011 recommendations of the WHO, which include terminating non-therapeutic use of antimicrobials and requiring obligatory prescriptions for all antimicrobials used for disease control in food-producing animals. Health Canada key informants reported that the Department is currently proceeding with a number of initiatives to address AMR and is collaborating with the PHAC, the CFIA, AAFC, and provincial/territorial authorities to develop a more coordinated approach to AMR.

Health Canada has been widely criticized by stakeholders for its failure to curtail the ongoing use of unapproved drugs, which is thought to be a major factor contributing to AMR. This practice is made possible by two features of the current regulatory framework for veterinary drugs. First, there is currently no prohibition against the import of unlicensed drugs for use on animals. This has enabled livestock producers to acquire less expensive veterinary products or products not available in Canada for use in their livestock operations. The other is current policies relating to active pharmaceutical ingredients (APIs), which are currently subject to minimal oversight by Health Canada. By comparison, other jurisdictions such as the EU and the US prohibit the importation and use of unlicensed veterinary drugs, and restrict the importation of bulk chemicals and APIs to holders of establishment licenses.

Recently, Health Canada has started the process to address OUI and the importation and direct use of APIs by holding stakeholder consultations on a proposed regulatory approach to OUI and APIs in March 2013.

## Recommendation 2

**Health Canada should continue to take measures to address the importation and use of unlicensed veterinary drugs and APIs.**

Health Canada's pharmacovigilance activities for veterinary drugs include monitoring of adverse drug reaction reports, signal detection, causality assessment, and post-market actions such as label changes and drug recalls. Stakeholders who participated in this evaluation identified a number of potential shortcomings of Health Canada's approach to adverse drug reaction reporting and post-market surveillance, including under-reporting of adverse drug reactions by end-users; lack of awareness and understanding of Health Canada's adverse drug reaction reporting requirements among foreign manufacturers; lack of adverse drug reaction reporting requirements for unapproved imported products, including APIs; lack of attention to product efficacy in adverse drug reaction reports, which key informants said is important in the context of AMR; and lack of post-market surveillance of vNHPs. Moreover, unlike the US and the EU, information on the number and types of veterinary drug adverse reactions is not publicly reported in Canada.

Compliance and enforcement activities relating to veterinary drugs are carried out by Health Canada and the CFIA, and include education, consultation, and information; compliance monitoring through GMP inspections and inspections for compliance with MRLs; compliance verifications and investigations; and the application of a variety of voluntary and/or regulatory compliance and enforcement measures in response to non-compliances. Health Canada's current approach to GMP inspections for veterinary drug establishments is perceived as problematic by the animal health products industry, which considers the Department to apply inappropriate guidelines stemming from a human health perspective to GMP inspections, including some that are not applied in the US or the EU. However, Health Canada has published specific guidance describing how GMP requirements may be applied differently in the case of veterinary drugs, and in recent consultations on a new regulatory framework for veterinary drugs, proposed that GMP requirements for veterinary drugs eligible under a proposed "registration" pathway would be introduced, similar to those prescribed in the *Natural Health Products Regulations.*

## Performance – achievement of outcomes

Over the evaluation period, Health Canada has engaged in many activities that should, in theory, contribute to the expected outcomes of the VDP. However, in most cases, administrative data to support conclusions on the extent to which outcomes have been achieved are limited. While the evaluation attempted to fill these gaps in information through the industry and end-user surveys, a small sample for the end-user survey resulted in limited reach and a low response rate. As a result of these factors, there are limited data on which to base definitive conclusions regarding achievement of outcomes.

In the immediate term, the VDP is expected to produce increased awareness and understanding by end-users of risks and benefits related to veterinary drugs, as well as increased awareness and understanding by industry of Health Canada's regulatory framework for veterinary drugs. While it seems clear that Health Canada has improved its communications and consultations with stakeholders in recent years, there is little evidence that these communications and consultations have produced the desired effect, particularly among end-users.

VDP activities are also intended to produce increased safety and effectiveness of veterinary drugs. The VDP contributes to product safety by establishing MRLs and AMRLs for veterinary drugs, and had established 269 maximum residue limits for 88 pharmacologically active substances as of May 2012. Furthermore, recent improvements in the submission review process could, in theory, lead to more safe and effective drugs on the market. However, there is no evidence that new drugs are, in fact, safer and more efficacious than existing products.

In the immediate term, VDP activities are intended to produce increased industry compliance with Health Canada's regulatory framework for veterinary drugs. There is some evidence that industry compliance with established MRLs and GMP requirements is generally high, but due to a shift to combined reporting for veterinary and human drug GMP inspections in 2007–08, it is difficult to discern clear trends in GMP compliance within the veterinary drug industry. As the regulatory agency responsible for veterinary drugs, it is important for Health Canada to track and report on compliance within the veterinary drugs industry. Such an approach is arguably more consistent with the Department's recent move to recognize the uniqueness of veterinary drugs through a new regulatory framework for veterinary drugs, and would also be more consistent with the approach taken by the FDA, which separates compliance reporting by product line. A greater focus in reporting on compliance outcomes (rather than activities and outputs) would also contribute to greater understanding of industry compliance.

## Recommendation 3

**Health Canada should undertake to improve reporting on industry compliance with the regulatory framework for veterinary drugs. Data for veterinary drug compliance and enforcement activities should be separated from data on human drug activities. Health Canada should also focus to a greater extent on compliance outcomes, as opposed to activities and outputs, in performance reporting.**

In the intermediate term, VDP activities are expected to lead external stakeholders to adopt safe behaviours associated with the use of veterinary drugs. There is some evidence from the literature that unsafe practices, including the use of antimicrobial agents, own-use importation, and importation and direct use of APIs, are taking place in Canadian agriculture, although the magnitude of the problem continues to be a matter of some debate. The impact of the VDP on end-user behaviour is an area for future research.

VDP activities are also expected to result, in the intermediate term, in increased use of scientific evidence and risk-benefit analysis by Health Canada to inform decision making. The use of scientific evidence and risk-benefit analysis is formally integrated into Health Canada's decision-making process, and, generally speaking, Health Canada appears to use scientific evidence and

risk-benefit analysis on a regular basis to inform decision making. However, the Department has not yet implemented regulatory reforms to address importation and use of unapproved drugs. This appears to be, at least in part, due to concerns about the potential economic impact of such reforms for livestock producers.

In the intermediate term, VDP activities are expected to produce a timely response to identified risks. In the absence of performance standards or information on the amount of time Health Canada has taken to respond to specific identified risks, there is insufficient evidence to support general conclusions on this outcome. However, there are a few examples of long-standing issues that Health Canada has, so far, not addressed through policy and regulatory change — in particular, the ongoing practice of importation and use of unapproved veterinary drugs.

VDP activities are also expected to lead, in the intermediate term, to increased international harmonization of regulatory frameworks for veterinary drugs and, ultimately, to improved human health and safety of the food supply. The evaluation evidence suggests that Health Canada has been active internationally. It participates in the VICH and the Codex Alimentarius Commission, and has established several agreements on information-sharing and regulatory cooperation with international counterparts. While regulatory harmonization initiatives such as these may have the potential to contribute to improved human health and safety of the food supply, in the absence of any concrete evidence, the health and safety benefits of increased harmonization are more theoretical than real.

In the long term, VDP activities are expected to contribute to reduced health risks and adverse events associated with the use of veterinary drugs, increased safety of Canada's food supply, and increased public confidence in veterinary drugs, the related regulatory system, and the food supply. It seems reasonable to assume that VDP activities such as timely approval of safe and efficacious drugs, prohibitions on the sale of certain products for use in food-producing animals for which no residue level is considered safe, management of drug residues in food, initiatives to influence the use of antimicrobial agents in food-producing animals, and post-market surveillance and compliance activities should, in theory, contribute to the safety of the food supply and reduced health risks. Addressing the ongoing importation and use of unapproved veterinary drugs would further contribute to risk reduction and food safety.

As for public confidence in veterinary drugs, the related regulatory system, and the food supply, recent public opinion surveys suggest that, at present, Canadians are quite confident in Canada's food safety system; that they generally approve of Canadian standards and regulations in the area of food safety; and also that confidence in the Government of Canada may contribute significantly to their confidence in the food safety system itself. However, there are no public opinion data pertaining specifically to veterinary drugs.

## Performance – efficiency and economy

Changes in HPFB's approach to financial reporting over the evaluation period made it challenging to compare and analyze this information over time. Furthermore, HPFB recently has begun including veterinary drugs in financial reporting on the larger Pharmaceutical Drugs Program. HPFB has the ability to isolate the veterinary drugs-related activities of the VDD from

its food safety-related activities for reporting. However, the VDP does not consist only of VDD activities, but also encompasses the activities of other program partners, such as the Inspectorate, RAPB, and RMOD. HPFB's current approach to financial reporting may not provide the total cost of the VDP. Furthermore, activity-based reporting, which is important to analysing program efficiency and economy, has not taken place since 2008-2009. From both a program management and an evaluation perspective, it is important to identify the total cost of the branch's veterinary drug-related activities and to analyze the cost drivers.

Due to significant weaknesses in the available financial and human resource information, the evaluation could not assess the extent to which program resources were used as planned, whether program outputs were produced efficiently, or whether expected outcomes were produced economically. That being said, there is evidence of improved operational efficiencies in recent years. The VDP has eliminated a considerable backlog of new drug submissions in recent years, drastically reduced the average time required to decide whether new drugs should be approved, and undertaken various other initiatives to improve the efficiency of pre-market review. Since many of these initiatives have been quite recent, their impact on program efficiency and economy has not yet been established. More extensive use of electronic submissions, acceptance of rolling submissions, acceptance of foreign data packages, and use of foreign reviews may introduce further efficiencies.

# Appendix A Evaluation Matrix

## Table 5: Evaluation of the Veterinary Drugs Program (VDP)

| Evaluation issues and questions | Indicators | Data sources |
|---|---|---|
| **SECTION 1: RELEVANCE** | | |
| **Issue #1: Continued need for the program** | | |
| 1. Is there a continued need for the VDP? | Need for program identified/documented | Document review:<br>Treasury Board submissions, Memoranda to Cabinet |
| | Evidence of current/emerging human health and food safety issues related to VDs | Literature review |
| | Expert/stakeholder assessment of ongoing need | Key informant interviews (internal and external) |
| **Issue #2: Alignment with government priorities** | | |
| 2. Is the VDP aligned with the priorities of the Government of Canada? | Extent to which program objectives are linked to federal government priorities | Document review:<br>recent Speeches from the Throne/Budgets<br>Food and Consumer Safety Action Plan RMAF<br>Growing Forward Framework Agreement and related documentation |
| | Extent to which program objectives are linked to the strategic outcomes/priorities of Health Canada/HPFB | Document review:<br>recent Health Canada Reports on Plans and Priorities |
| **Issue #3: Alignment with federal roles and responsibilities** | | |
| 3. Is the VDP consistent with federal roles and responsibilities? | Extent to which the program objectives are consistent with the legislative framework of the federal government | Document review:<br>federal Acts and Regulations (*Food and Drugs Act*, *Health of Animals Act*, *Feeds Act* and their respective Regulations) |
| | Extent to which the program objectives are consistent with the legislative framework of Health Canada | Document review:<br>federal Acts and Regulations (*Food and Drugs Act and Regulations*)<br>recent Health Canada Reports on Plans and Priorities<br>VDD, Inspectorate, and HPFB Operational and Strategic Plans |
| **SECTION 2: PERFORMANCE (EFFECTIVENESS, EFFICIENCY, ECONOMY)** | | |
| **Issue #4: Achievement of expected outcomes** | | |
| 4. Is the Program's governance structure likely to support the achievement of expected outcomes? | | |

| Evaluation issues and questions | Indicators | Data sources |
|---|---|---|
| a) Is there an established governance structure to coordinate VDP delivery? | Extent to which internal and interdepartmental partners' roles, responsibilities, accountabilities, and decision-making authorities are documented and understood | Document review:<br>- descriptions of the organizational structures, mandates and activities of program partners, as available from the following:<br>o Health Canada and CFIA websites<br>o VDD, Inspectorate, and HPFB Strategic and Operational Plans<br>o other internal documentation<br>- Food and Consumer Safety Action Plan RMAF<br>- Growing Forward MoU with AAFC (Veterinary Drugs Initiative)<br>- Border Integrity Approach Policy Document<br>Key informant interviews (internal and external, i.e., other federal departments) |
| | Nature of industry involvement in VDP governance | Document review:<br>- Minutes of meetings/reports of consultations with industry stakeholders (e.g., CAHI, CAHPRAC)<br>Key informant interviews (internal and external) |
| | Extent of collaboration among internal and interdepartmental partners, as evidenced by:<br>- existence of committees, working groups, and teams<br>- frequency of meetings of committees, working groups, and teams | Document review<br>- VDD, Inspectorate, and HPFB Operational and Strategic Plans and performance reporting<br>- CIPARS-related documentation<br>- committee/working group Terms of Reference (as available)<br>- meeting agendas/minutes (as available)<br>Key informant interviews (internal and external, i.e. other federal departments) |
| b) Has a performance measurement framework been designed and implemented? | Existence of performance measurement framework(s) | Document review<br>- VDD performance reports, FY 2003–04 to 2010–11 (including Submission Review Performance Measures)<br>- Inspectorate draft performance indicators, FY 2009–10<br>- HPFB performance reports (including public involvement performance reports, FY 2004–05 to 2006–07 & FY 2009–10 to 2010–11<br>- Food and Consumer Safety Action Plan RMAF<br>- Growing Forward MoU with AAFC (Veterinary Drugs Initiative) |
| | Extent to which performance data are collected | Document review<br>- VDD performance reports, FY 2003–04 to 2010–11 (including Submission Review Performance Measures)<br>- Inspectorate draft performance indicators, FY 2009–10<br>- HPFB performance reports (including public involvement performance reports), FY 2004–05 to 2006–07 & FY 2009–10 to 2010–11<br>- Health Canada DPRs<br>- Progress on Food Safety reports<br>- Report on VDD-AAFC Growing Forward Regulatory Action Plan, 2008–2009<br>Key informant interviews (internal) |

| Evaluation issues and questions | Indicators | Data sources |
|---|---|---|
| c) Is the performance measurement framework used to support decision making? | Extent to which performance data are used to support decision making | Document review<br>- VDD, Inspectorate, and HPFB Operational and Strategic Plans and performance reporting<br>- Other management planning documents (if available)<br>Key informant interviews (internal) |
| 5. To what extent has the VDP been implemented as planned? | | |
| a) Has the Program effectively addressed challenges, emerging issues, and changing priorities? | Extent to which challenges, emerging issues, and changing priorities were effectively addressed, for example:<br>- Extra label drug use (ELDU)<br>- Own use importation (OUI)<br>- Submission review timelines<br>- Antimicrobial resistance (AMR)<br>- Maximum residue limits (MRLs)<br>- Minor use, minor species (MUMS)<br>- Veterinary natural health products | Document review<br>- VDD performance reports, FY 2003–04 to 2010–11 (including Submission Review Performance Measures)<br>- VDD, Inspectorate, and HPFB Operational and Strategic Plans and performance reporting<br>- Issue Analysis documents<br>- Communications/consultations with stakeholders including reports of such consultations<br>- Policies, regulations, and guidelines implemented to address challenges, emerging issues, and changing priorities<br>Key informant interviews (internal and external)<br>Key issues |
| b) Have activities been implemented as planned? | Extent to which VDP activities were implemented as planned | Document review:<br>For planned implementation:<br>- Treasury Board submissions<br>- Memoranda to Cabinet<br>- VDD, Inspectorate, and HPFB Operational and Strategic Plans<br>- Food and Consumer Safety Action Plan RMAF<br>- Growing Forward MoU with AAFC (Veterinary Drugs Initiative)<br>For actual implementation:<br>- VDD performance reports, FY 2003–04 to 2010–11 (including Submission Review Performance Measures)<br>- Inspectorate draft performance indicators, FY 2009–10<br>- HPFB performance reports (including public involvement performance reports), FY 2004–05 to 2006–07 & FY 2009–10 to 2010–11<br>- Health Canada DPRs<br>- Progress on Food Safety reports<br>- Report on VDD-AAFC Growing Forward Regulatory Action Plan, 2008–2009<br>- Actual spending data<br>Key issues |

| Evaluation issues and questions | Indicators | Data sources |
|---|---|---|
| c) Have the activities produced the expected outputs? | Enumeration of outputs (e.g., policies, guidelines, regulations, research, MoUs) produced for each activity | Document review:<br>For expected outputs:<br>- Treasury Board submissions<br>- Memoranda to Cabinet<br>- VDD, Inspectorate, and HPFB Operational and Strategic Plans<br>- Food and Consumer Safety Action Plan RMAF<br>- Growing Forward MoU with AAFC (Veterinary Drugs Initiative)<br>For actual outputs:<br>- VDD performance reports, FY 2003–04 to 2010–11 (including Submission Review Performance Measures)<br>- Inspectorate draft performance indicators, FY 2009–10<br>- HPFB performance reports (including public involvement performance reports), FY 2004–05 to 2006–07 & FY 2009–10 to 2010–11<br>- Health Canada DPRs<br>- Progress on Food Safety reports<br>- Report on VDD-AAFC Growing Forward Regulatory Action Plan, 2008–2009<br>- Policies, guidelines, regulations, research, MoUs, etc.<br>Key issues |
| d) Have requirements/commitments to Central Agencies (i.e., Office of the Auditor General, Cabinet Directive on Streamlining Regulations, Policy on Public Consultation, Policy on Gender-Based Analysis) been addressed? | Extent to which requirements and commitments to Central Agencies have been addressed | Document review (extent to which relevant documents may be available)<br>Key informant interviews (internal and external) |
| 6. To what extent has progress towards expected outcomes been achieved? | | |
| **Immediate outcomes** | | |
| a) To what extent is there increased awareness and understanding among external stakeholders of risks and benefits related to veterinary drugs? | Extent and nature of Health Canada communications to and consultations with external stakeholders regarding risks and benefits of VDs | Document review:<br>- Health Canada communications, meetings, and consultations with stakeholders regarding risks and benefits of VDs |
| | External stakeholder perceptions of their level of awareness and understanding of risks and benefits related to VDs | Key informant interviews (external)<br>Survey of stakeholders<br>Key issues |
| b) To what extent is there increased awareness and understanding among industry of Health Canada's regulatory framework for veterinary drugs? | Extent and nature of Health Canada communications to/consultations with industry regarding the regulatory framework for veterinary drugs | Document review:<br>- Health Canada communications, meetings, and consultations with stakeholders regarding the regulatory framework for veterinary drugs |
| | Industry perceptions of its level of awareness and understanding of Health Canada's regulatory framework for VDs | Key informant interviews (external)<br>Survey of industry<br>Key issues |

| Evaluation issues and questions | Indicators | Data sources |
|---|---|---|
| c) To what extent is there increased safety and effectiveness of veterinary drugs? | Proportion of veterinary drug submissions processed within service standards and targets | Administrative data review:<br>- VDD submission review performance data |
| | Trend data on number and proportion of veterinary drug submissions and Clinical Trial Authorizations approved/refused at various stages of review process | Administrative data review:<br>- SKMD submission and approval data (if available) |
| | Number and proportion of entities for which MRLs have been established from prioritized list | Administrative data review:<br>- HSD data on established MRLs |
| | External and internal stakeholder perceptions of safety and effectiveness of VDs, including perceptions of adequacy of processes in place to ensure safety and effectiveness | Literature review<br>Document review, for example:<br>- Proceedings of Standing Committee on Health<br>Key informant interviews (internal and external)<br>Survey of industry and stakeholders<br>Key issues |
| d) To what extent is there increased industry compliance with Health Canada's regulatory requirements related to veterinary drugs? | Trends in percentage of veterinary drug submissions and Clinical Trial Applications that receive Notices of Deficiency and/or Notices of Non-Compliance | Administrative data review :<br>- SKMD submission and approval data (if available) |
| | Trends in compliance and enforcement actions taken (e.g., number of VDs removed from market) | Administrative data review:<br>- Inspectorate data (if available) |
| | Trends in percentage of inspected/verified registrants/firms in compliance with regulatory framework | Administrative data review:<br>- Inspectorate data (if available)<br>Document review:<br>- Health Canada Departmental Performance Reports (DPRs) |
| | number of import alerts resulting in detecting/stopping non-compliant products at the border (FCSAP indicator related to Strategy #10) | Administrative review:<br>- Inspectorate data (if available) |
| | Extent to which industry is compliant with MRLs | Document review:<br>- National Chemical Residues Monitoring Program annual reports |
| | Industry self-report data related to compliance and enforcement | Survey of industry<br>Key informant interviews (external — industry representatives) |
| **Intermediate outcomes** | | |
| e) To what extent do external stakeholders adopt safe behaviours associated with veterinary drugs? | Extent to which external stakeholders report using Health Canada publications, advisories, guidance, policies, and regulations for decision making | Key informant interviews (external)<br>Survey of industry and stakeholders |
| | Extent of reported incidents of improper or unsafe use of VDs | Key informant interviews (external, especially representatives of provincial veterinary associations for usage information)<br>Survey of stakeholders<br>Key issues |
| f) To what extent is there increased use of scientific evidence and risk- | Composition of expert/scientific advisory groups (researchers/academics, industry, etc.) | Document review:<br>- Terms of Reference and membership lists of advisory groups |

| Evaluation issues and questions | Indicators | Data sources |
|---|---|---|
| benefit analysis by Health Canada to inform decision making? | Extent to which recommendations of expert/scientific advisory groups are used to inform/develop policy/regulatory responses | Document review:<br>- Terms of Reference, meeting minutes, and reports/recommendations of expert/scientific advisory groups<br>- Policies, guidelines, regulations |
| | Extent to which regulatory changes include Regulatory Impact Analysis (RIA) statements | Document review:<br>- RIAs in *Canada Gazette* |
| | Comprehensiveness of data used in pre-market review | Document review (if available)<br>Key informant interviews (internal) |
| | Use of international post-market data to inform pre-market review | Document review (if available)<br>Key informant interviews (internal) |
| | Extent to which safety signals and adverse drug reactions (ADRs) are monitored and used to inform decision making | Administrative data review — CED data:<br>- Annual summary reports on ADRs<br>- Summaries of post market information<br>- Safety update summaries<br>Key informant interviews (internal) |
| | Extent to which Health Risk Assessments are developed in response to non-compliance | Document review (HRAs, if available)<br>Key informant interviews (internal) |
| | Evidence that information gathered through post-market events is used to inform decision making | Document review (if available)<br>Key informant interviews (internal) |
| | Stakeholders' perceptions of extent to which use of scientific evidence and risk-based analysis to inform decision making has increased | Key informant interviews (external and internal)<br>Survey of stakeholders |
| g) To what extent is there a timely regulatory system response to identified risks? | Elapsed time between initial identification of risk and policy/regulatory response | Document review (if information is available) |
| | Internal and external stakeholder perceptions of timeliness of Health Canada's response to identified risks associated with VDs | Key informant interviews (external and internal)<br>Survey of industry and stakeholders<br>Key issues |
| h) To what extent has international harmonization of regulatory frameworks for veterinary drugs contributed to improved health of Canadians and increased safety of Canada's food supply? | Extent to which main features of Canada's regulatory framework for VDs is harmonized with that of other jurisdictions | Literature review:<br>- comparison of main features of Canada's regulatory framework with that of selected other jurisdictions (EU, US)<br>Key issues<br>Key informant interviews (internal and external) |
| | Internal and external stakeholder perceptions of impact of international harmonization on health of Canadians and safety of food supply | Literature review<br>Key informant interviews (internal and external) |

| Evaluation issues and questions | Indicators | Data sources |
|---|---|---|
| **Long-term outcomes** | | |
| i) To what extent have health risks and adverse events associated with the use of veterinary drugs been reduced? | Trends in veterinary drug-related illnesses and adverse drug reactions (ADRs) | Document/administrative data review:<br>- PHAC surveillance reports<br>- Annual summary reports on ADRs<br>- Summaries of post market information<br>- Safety update summaries<br>- Health Canada DPRs<br>- CFIA data (if available) |
| | Expert assessment of changes in health risks | Key informant interviews (internal and external)<br>Literature review |
| j) To what extent has the VDP contributed to the safety of Canada's food supply? | Key informant/expert opinion of extent to which the VDP has contributed to the safety of Canada's food supply | Key informant interviews (internal and external)<br>Literature review |
| k) To what extent is there increased public confidence in veterinary drugs, the related regulatory system, and the food supply? | Level of public confidence in safety of VDs, the related regulatory system, and the food supply | Document review:<br>- Health Canada public opinion research (if available)<br>- Health Canada DPRs<br>- AAFC public opinion surveys<br>Key informant interviews (external) |
| l) To what extent is there a sustainable, cost-efficient, responsive and science-based regulatory system for veterinary drugs in Canada? | Cumulative evidence from all outcome indicators | All data sources |
| m) Were there any unintended consequences, either positive or negative, of the program? | Unintended consequences identified by internal and external stakeholders<br>Unintended consequences identified through documents/literature | Key informant interviews (internal and external)<br>Document and literature review |
| **Issue #5: Efficiency and Economy** | | |
| 7. Were Program resources used as planned? What accounted for overruns or lower than planned expenditures? | Comparison of planned versus actual spending for components of VDP and explanations for variances | Administrative data review:<br>- e.g., planned versus actual spending, SAP data, financial derivation reports, management variance reports (if available)<br>Key informant interviews (internal) |
| 8. Are there lower-cost approaches to producing Program outputs? | Extent to which existing resources could be used to produce outputs at lower cost<br>Availability/accessibility of other, lower cost resources to produce outputs | Key informant interviews (internal)<br>Document review |
| 10. Are there alternate ways to achieve similar results at lower cost? | Approaches used in other jurisdictions and their costs<br>Internal and external stakeholder assessment of other options | Literature review<br>Key informant interviews (internal and external)<br>Key issues |

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# Appendix C Supplementary data tables

**Table 1: Findings of studies on impact of AMR infections**

| Study author(s) and year | Findings |
|---|---|
| Martin et al. (2004) | Using data from 440 cases of *Salmonella enterica* identified in Canada between December 1999 and November 2000, the authors find that hospitalization was likelier to occur among patients whose infections were resistant to ampicillin, chloramphenicol, and/or kanamycin, streptomycin, sulphamethoxazole, and tetracycline, compared to patients whose infections were susceptible to these agents. |
| Helms, Vastrup, Gerner-Smidt, and Mølbak (2002) | Using a matched cohort methodology, the authors find that while Danish patients with strains of *Salmonella typhimurium* susceptible to treatment with antibiotics were 2.3 times likelier than the general population to die within two years, patients with strains resistant to ampicillin, chloramphenicol, streptomycin, sulphonamide, and tetracycline were 4.8 times likelier to die; resistance to quinolone increased the relative risk ratio to 10.3 times the likelihood of death, compared to the general population. |
| Birnbaum, Jandciu, and Twells (2002) | The authors estimate that drug-resistant infections have increased health care costs in Canada by $14.2–$25.5 million annually due to higher hospitalization costs. They further estimate that screening to detect carriers of resistant organisms would increase annual costs by $10.3 million, while quarantining carriers would cost an additional $15.9 million. Were Canada's level of drug resistance to increase to the levels then present in the US, Birnbaum et al. (2002) estimate that the annual costs of hospitalization alone would be expected to rise by $103.9–$187.1 million. |
| Goetghebeur, Landry, Han, & Vicente (2007) | The authors cite results from the Canadian Nosocomial Infection Surveillance Program (CNISP) suggesting a tenfold increase in incidence of methicillin-resistant *staphylococcus aureus* (MRSA) in Canadian hospitals between 1995 and 2004 (p. 27). They estimate an average cost of $12,216 (2005 dollars) per patient infected with MRSA (primarily due to the cost of hospitalization), implying a total direct health care cost to Canada of $82 million in 2004; on the basis of historical increases in costs attributable to MRSA, they project costs to the health care system of $129 million in 2010 (Goetghebeur et al., 2007, p. 31). They note that these figures are likely conservative, since they do not account for community-associated MRSA (CA-MRSA), the costs of outbreak management, or indirect costs (pp. 31-32). |

**Table 2: Findings of studies on presence of antimicrobial-resistant bacteria in food supply due to animal-based food products**

| Study author(s) and year | Findings |
|---|---|
| PHAC (2011) | The 2008 CIPARS identified occurrences of ciprofloxacin-resistant *E. coli* in retail chicken and pork. A recent CIPARS surveillance bulletin identified a significant increase in prevalence in ciprofloxacin-resistant *Campylobacter* in retail chicken in British Columbia and Saskatchewan. Ciprofloxacin is a fluoroquinolone antimicrobial, which is considered very important to human medicine (PHAC, 2011, p. 92). |
| NARMS (2009) | The US-based National Antimicrobial Resistance Monitoring System (NARMS) recently found resistant bacteria in retail chicken, ground turkey, ground beef, and pork chops. |
| Enne, Cassar, Sprigings, Woodward, & Bennett (2008); Little, Richardson, Owen, de Pinna, & Threlfall (2008); Sheridan, Blair, & McDowell (1998) | These authors have reported findings of antimicrobial-resistant bacteria in retail and abattoir meats in the UK. |

**Table 3: Components of a veterinary drug submission**

| Component | Description |
|---|---|
| Master volume | Includes, among other elements, a cover letter and table of contents, a completed submission certification form, authorization letters, drug submission and submission fee application forms, animal ingredient forms, draft product labels, and patent forms and documents. |
| Manufacturing and quality control section | Includes detailed information about the drug substance and the drug product (these are not synonymous), such as nomenclature, chemical structure, physicochemical properties, method of manufacture, structure elucidation and confirmation, impurities, reference standards, packaging, and stability. |
| Animal safety section | Consists of information relating to laboratory animal studies and target animal safety studies. In each case, a wide variety of information is required; for example, submission content related to laboratory animal studies includes acute, sub-chronic, and chronic toxicity studies; irritation studies; and reproduction and teratogenicity studies. |

| Component | Description |
|---|---|
| Product efficacy section | Consists of results from microbiology, laboratory, animal model efficacy, and clinical pharmacology studies, as well as dose determination and confirmation studies. |
| Human safety section | Divided into three sub-sections examining laboratory animal toxicity, microbiological safety, and residues. This section of the submission is intended to address such questions as the impact of new antimicrobials on human gut microflora and human medicine, as well as the potential impact on consumers of ingesting veterinary drug residues and the time required for drug residues in animal tissues or products to fall beneath MRLs. |
| Environmental impact section | Relates to the New Substances Notification Regulation of the *Canadian Environmental Protection Act* |

Source: (VDD, 2007b).

**Table 4: MoRS targets for veterinary drug submissions**

| Submission class | Target in days | | | | |
|---|---|---|---|---|---|
| | Screening 1 | Screening 2 | Review 1 | Review 2 | Total |
| New Drug Submission | 45 | 45 | 300 | 150 | 540 |
| Abbreviated New Drug Submission | 45 | 45 | 300 | 150 | 540 |
| Supplemental New Drug Submission | 45 | 45 | 240 | 120 | 450 |
| Supplemental Abbreviated New Drug Submission | 45 | 45 | 240 | 120 | 450 |
| Administrative New Drug Submission | 14 | 14 | 90 | 45 | 163 |
| Administrative Abbreviated New Drug Submission | 14 | 14 | 90 | 45 | 163 |
| Notifiable Change Submission | N/A | N/A | 90 | N/A | 90 |
| Investigational New Drug Submission | N/A | N/A | 60 | N/A | 60 |
| Experimental Study Certificate Submission | N/A | N/A | 60 | N/A | 60 |
| Drug Identification Number Submission | N/A | N/A | 120 | N/A | 120 |
| Emergency Drug Release Submission* | N/A | N/A | N/A | N/A | N/A |

* For EDR Submissions, the MoRS target is for 100% to be completed within 48 hours.
**Source:** HPFB (2010c)

**Table 5: VDD submission review performance to targets, Q1 FY 2008-09 to Q4 FY 2010-11**

| Type of submission, screening and review | | | FY 2008–09 | | | | FY 2009–10 | | | | FY 2010–11 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Q1 | Q2 | Q3 | Q4 | Q1 | Q2 | Q3 | Q4 | Q1 | Q2 | Q3 | Q4 |
| NDS | Screening | 1 | Y | Y | Y | Y | N | Y | N | Y | N | N | N | Y |
| | | 2 | Y | Y | Y | Y | NC | NC | Y | Y | Y | Y | Y | N |
| | Review | 1 | NC | NC | NC | NC | N | N | N | N | N | N | Y | N |
| | | 2 | NC | NC | NC | NC | NC | NC | N | N | Y | N | N | Y |
| ANDS | Screening | 1 | N/A | N | Y | Y | Y | Y | N/A | Y | N | N | N | Y |
| | | 2 | Y | Y | N/A | N/A | NC | NC | N/A | N/A | Y | N/A | N/A | N/A |
| | Review | 1 | NC | NC | NC | NC | Y | N | Y | Y | N | Y | N/A | N |
| | | 2 | NC | NC | NC | NC | NC | NC | N/A | N/A | N/A | N | N/A | N/A |
| SNDS | Screening | 1 | Y | Y | Y | Y | Y | Y | Y | N/A | Y | Y | N | N |
| | | 2 | Y | Y | Y | N/A | NC | NC | N/A | Y | N/A | N/A | N/A | N/A |
| | Review | 1 | NC | NC | NC | NC | Y | N | Y | N | N | N | N | N |
| | | 2 | NC | NC | NC | NC | NC | NC | N | N/A | Y | N/A | N/A | N/A |
| SANDS | Screening | 1 | N/A | N/A | N/A | Y | N/A | N/A | Y | N/A | N/A | Y | Y | N |
| | | 2 | N/A | N/A | N/A | N/A | NC | NC | N/A | N/A | N/A | N/A | N/A | N/A |
| | Review | 1 | NC | NC | NC | NC | N/A | N/A | Y | Y | Y | N/A | N/A | N |
| | | 2 | NC | NC | NC | NC | NC | NC | N/A | N/A | N/A | N/A | N/A | N/A |
| Admin NDS | Screening | 1 | N | Y | N/A | Y | NC | NC | N | Y | Y | N | Y | Y |

| Type of submission, screening and review | | | FY 2008–09 | | | | FY 2009–10 | | | | FY 2010–11 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Q1 | Q2 | Q3 | Q4 | Q1 | Q2 | Q3 | Q4 | Q1 | Q2 | Q3 | Q4 |
| | | 2 | N/A | N/A | N/A | Y | NC | NC | Y | Y | N/A | N/A | N/A | N/A |
| | Review | 1 | NC | NC | NC | NC | NC | NC | N | N | N | N | Y | N |
| | | 2 | NC | NC | NC | NC | NC | NC | Y | N | N | N/A | N/A | N/A |
| Admin ANDS | Screening | 1 | N/A | N/A | N/A | N/A | NC | NC | N/A | N/A | N/A | N/A | N/A | N/A |
| | | 2 | N/A | N/A | N/A | N/A | NC | NC | N/A | N/A | N/A | N/A | N/A | N/A |
| | Review | 1 | NC | NC | NC | NC | NC | NC | N/A | N/A | N/A | N/A | N/A | N/A |
| | | 2 | NC | NC | NC | NC | NC | NC | N/A | N/A | N/A | N/A | N/A | N/A |
| NC (Review 1) | | | NC | NC | NC | NC | NC | NC | N | N | N | N | N | N |
| IND (Review 1) | | | N/A | N/A | N/A | N/A | NC | NC | N/A | N/A | Y | N/A | N | N/A |
| ESC (Review 1) | | | Y | Y | Y | Y | NC | NC | Y | Y | Y | Y | N | Y |
| DIN (Review 1) | | | N | N | Y | Y | NC | NC | N | N | Y | N | N | N |
| EDR (Review 1) | | | Y | Y | Y | Y | NC | NC | Y | Y | Y | Y | Y | Y |
| **Number of targets met** | | | **7/9** | **8/10** | **8/8** | **10/10** | **4/6** | **3/6** | **10/18** | **10/17** | **11/19** | **6/16** | **6/15** | **6/16** |
| **% of targets met** | | | **77.8** | **80.0** | **100.0** | **100.0** | **66.7** | **50.0** | **55.6** | **58.8** | **57.9** | **37.5** | **40.0** | **37.5** |

**NOTE:** **Y** cells represent targets successfully achieved, while **N** cells represent targets which were not achieved. NC reflects data which was not collected in a particular quarter.

**Adapted from:** HPFB (2010c); (2008b, 2008c, 2009d, 2009e, 2009f, 2009g, 2010b, 2010c, 2010d, 2011f, 2011g)

**Table 6: Industry views on Health Canada's consultations**

| Industry Views | n=10 | | | |
|---|---|---|---|---|
| | Agree | Neutral | Disagree | Don't know |
| Health Canada has consulted adequately with the veterinary drug industry over the past 10 years | 7 | 1 | 2 | - |
| Health Canada's existing consultation mechanisms provide an effective means for the veterinary drug industry to express their concerns and interests to Health Canada | 6 | 3 | 1 | - |
| Over the past 10 years, Health Canada has taken the concerns and interests of the veterinary drug industry into account in policy and regulatory development | 3 | 3 | 4 | - |
| Pre-submission meetings are an effective mechanism for ensuring that product submissions meet Health Canada's requirements | 9 | 1 | - | - |
| My organization is aware of the Veterinary Drugs Directorate's process for dispute resolution during the product submission process | 5 | 2 | 3 | - |

**Table 7: End-user views on Health Canada's consultations**

| End-user views | n=21 | | | |
|---|---|---|---|---|
| | Agree | Neutral | Disagree | Don't know |
| Health Canada has consulted adequately with veterinary drug end-users over the past 10 years | 5 | 5 | 5 | 6 |
| Health Canada's existing consultation mechanisms provide an effective means for veterinary drug end-users to express their concerns and interests to Health Canada | 6 | 3 | 7 | 5 |
| Over the past 10 years, Health Canada has taken the concerns and interests of veterinary drug end-users into account in policy and regulatory development | 2 | 7 | 5 | 7 |

**Table 8: End-user rating of understanding of risk and safety information relevant to veterinary drugs**

| End-user rating | n=21 | | |
|---|---|---|---|
| | Strong | Moderate | Poor |
| Risk management measures to address antimicrobial resistance associated with the use of antimicrobial agents in food-producing animals | 14 | 4 | 3 |
| Potential human health risks of antimicrobial resistance related to the use of antimicrobial agents in food-producing animals | 13 | 7 | 1 |
| Health Canada's Policy on ELDU | 13 | 5 | 3 |
| Prudent use of veterinary drugs in livestock feeds | 12 | 6 | 3 |
| MRLs for food-producing animals | 10 | 7 | 4 |
| Potential human health risks of ELDU in food-producing animals | 9 | 6 | 6 |
| Potential animal and human health risks related to use of unapproved drugs, including compounding and direct use of APIs | 8 | 9 | 4 |
| Potential human health risks associated with the use of hormonal growth promoters in food-producing animals | 5 | 11 | 5 |
| How and when to report an ADR | 4 | 12 | 5 |

**Table 9: End-user awareness and use of Health Canada information**

| Type of information | n=21 | |
|---|---|---|
| | Aware of information | Used information |
| Information on MRLs for food-producing animals | 19 | 10 |
| Health Canada's Policy on ELDU | 17 | 11 |
| Information on the potential human health risks of antimicrobial resistance related to the use of antimicrobial agents in food-producing animals | 16 | 7 |
| Risk management measures to address antimicrobial resistance associated with the use of antimicrobial agents in food-producing animals | 15 | 9 |
| Information on the prudent use of veterinary drugs in livestock feeds | 15 | 6 |
| Information on how and when to report an ADR | 15 | 4 |
| Information on the potential human health risks of ELDU in food-producing animals | 14 | 6 |
| Information on ADRs, warnings, and/or recalls related to specific veterinary drugs | 14 | 3 |
| Information on potential animal and human health risks related to use of unapproved drugs, including compounding and direct use of APIs | 12 | 2 |
| Information on the potential human health risks associated with the use of hormonal growth promoters in food-producing animals | 10 | 1 |

**Table 10: Level of end-user agreement with statements about Health Canada's impact on understanding**

| End-user level of understanding | n=21 | | | |
|---|---|---|---|---|
| | Agree | Neutral | Disagree | Don't know |
| Overall, Health Canada has influenced my understanding of animal health risks related to veterinary drugs | 7 | 8 | 4 | 2 |
| Overall, Health Canada has influenced my understanding of human health risks related to veterinary drugs | 7 | 5 | 7 | 2 |

**Table 11: Industry rating of understanding of Health Canada's regulations, policies, and activities**

| Health Canada regulation, policy, activity… | n=10 | | |
|---|---|---|---|
| | Strong | Moderate | Poor |
| Health Canada's submission requirements for veterinary drugs | 7 | 2 | 1 |
| Health Canada's requirements related to GMP for manufacturers of veterinary drugs | 5 | 5 | - |
| Health Canada's requirements related to establishment licensing for manufacturers of veterinary drugs | 5 | 4 | 1 |
| Health Canada's requirements for mandatory ADR reporting for veterinary drugs | 5 | 2 | 3 |
| Health Canada's regulatory compliance activities, including inspections and compliance verifications, and related enforcement actions to address identified risks (i.e., non-compliances) | 1 | 6 | 3 |

**Table 12: Industry awareness and use of Health Canada information**

| Type of information | (n=10) | |
|---|---|---|
| | Aware of information | Used information |
| Information on Health Canada's submission requirements for veterinary drug manufacturers applying to have a new product approved for sale in Canada | 10 | 9 |
| Information on Health Canada's requirements related to GMP for manufacturers of veterinary drugs | 10 | 9 |
| Information requirements related to establishment licensing for manufacturers of veterinary drugs | 10 | 8 |
| Information on Health Canada's requirements for mandatory ADR reporting for veterinary drugs | 10 | 8 |
| Information on the electronic submission process for veterinary drugs | 9 | 3 |
| Information on Health Canada's regulatory compliance activities, including inspections and compliance verifications, and related enforcement actions to address identified risks | 7 | 6 |

**Table 13: Level of industry agreement with statements about Health Canada's ADR reporting requirements**

| Industry level of understanding | (n=10) | | | |
|---|---|---|---|---|
| | Agree | Neutral | Disagree | Don't know |
| Health Canada has clearly outlined the time frame for mandatory ADR reporting | 8 | - | 1 | 1 |
| Health Canada has clearly outlined what information must be included by manufacturers/what information end-users are encouraged to include | 6 | 2 | 2 | - |
| Health Canada has clearly identified where within the department manufacturers must submit ADR reports/where within the department end-users should submit ADR reports | 6 | 2 | 2 | - |
| Health Canada has clearly identified where within the department manufacturers must submit ADR reports/where within the department end-users should submit ADR reports | 5 | 2 | 3 | - |
| In the event of an ADR that had to be reported, my firm could provide all of the information required by Health Canada* | 6 | 1 | 1 | - |
| In the event of an ADR that had to be reported, my firm could complete a mandatory ADR report in the required time frame* | 5 | 2 | 1 | - |

* Note: The industry sample size for this statement is 8.

**Table 14: Level of end-user agreement with statements on Health Canada's ADR reporting requirements**

| End-user level of understanding | n=21 | | | |
|---|---|---|---|---|
| | Agree | Neutral | Disagree | Don't know |
| Health Canada has clearly outlined what information end-users are encouraged to include | 7 | 4 | 1 | 9 |
| Health Canada has clearly identified where within the department end-users should submit ADR reports | 5 | 5 | 1 | 10 |
| Health Canada has clearly defined what ADRs end-users are encouraged to report | 8 | 2 | 2 | 9 |

**Table 15: Level of end-user agreement with statements about Health Canada's impact on understanding and behaviour**

| End-user level of agreement | n=21 | | | |
|---|---|---|---|---|
| | Agree | Neutral | Disagree | Don't know |
| Overall, Health Canada has influenced my understanding of animal health risks related to veterinary drugs | 7 | 8 | 4 | 2 |
| Overall, Health Canada has influenced my understanding of human health risks related to veterinary drugs | 7 | 5 | 7 | 2 |
| Health Canada's policies and risk communications have influenced the way in which I practise veterinary medicine and/or use veterinary drugs | 7 | 6 | 4 | 4 |

**Table 16: Level of industry and end-user agreement with statements about Health Canada's use of scientific evidence and risk analysis**

| Level of Agreement | Industry (n=10) | | | | End-users (n=21) | | | |
|---|---|---|---|---|---|---|---|---|
| | Agree | Neutral | Disagree | Don't know | Agree | Neutral | Disagree | Don't know |
| Health Canada's policies and regulations related to veterinary drugs are based on best available scientific evidence | 4 | 4 | 2 | - | 11 | 3 | 1 | 6 |
| Health Canada's policies and regulations related to veterinary drugs are based on an appropriate analysis of risk | 3 | 3 | 4 | - | 11 | 3 | 1 | 6 |

**Table 17: Level of industry and end-user agreement with statement about timeliness of Health Canada's response to risk**

| Level of Agreement | Industry (n=10) | | | | End-users (n=21) | | | |
|---|---|---|---|---|---|---|---|---|
| | Agree | Neutral | Disagree | Don't know | Agree | Neutral | Disagree | Don't know |
| Overall, in the past 10 years, Health Canada has responded in a timely manner to identified risks related to veterinary drugs | 2 | 2 | 4 | 2 | 4 | 6 | 2 | 9 |

**Table 18: Number of enforcement actions related to veterinary drugs, FY 2003–04 to 2006–07**

| Fiscal year | Seizures made | Prosecutions initiated | Voluntary disposals* | Voluntary detentions^ | All actions |
|---|---|---|---|---|---|
| 2003–04 | 0 | 0 | 1 | 2 | 3 |
| 2004–05 | 0 | 0 | 0 | 1 | 1 |
| 2005–06 | 0 | 0 | 0 | 3 | 3 |
| 2006–07 | 0 | 0 | 0 | 0 | 0 |
| **Total** | **0** | **0** | **1** | **6** | **7** |

Sources: Inspectorate (2004, 2005b, 2006, 2007c, 2008, 2009b, 2010b)

* A voluntary disposal is "an action by a regulated party to prevent further distribution of a non-compliant product, by actions such as disposal, destruction, reconditioning, or returning it to the manufacturer" (Inspectorate, 2005a).

^ A voluntary detention is "an agreement between a regulated party and Health Canada [for the regulated party] to maintain control of a particular product" (Inspectorate, 2005a).

**Table 19: Number of veterinary drug recalls by hazard type, FY 2003–04 to 2010–11**

| Fiscal year | Type I | Type II | Type III | Not classified | Total |
|---|---|---|---|---|---|
| 2003–04 | 0 | 5 | 5 | 0 | 10 |
| 2004–05 | 0 | 5 | 7 | 0 | 12 |
| 2005–06 | 1 | 3 | 4 | 0 | 8 |
| 2006–07 | 1 | 0 | 2 | 0 | 3 |
| 2007–08 | 0 | 0 | 0 | 0 | 0 |
| 2008–09 | 0 | 1 | 2 | 0 | 3 |
| 2009–10 | 2 | 11 | 0 | 0 | 13 |
| 2010–11 | 1 | 0 | 4 | 3 | 8 |
| **Total** | **5** | **25** | **24** | **3** | **57** |

Sources: Inspectorate (2004, 2005b, 2006, 2007c, 2008, 2009b, 2010b). Data for 2010-11 provided by Health Canada.

**Table 20: Veterinary drug shipments referred to the Inspectorate for examination, Q1, FY 2009–10 to Q4, 2010–11**

| Fiscal year | Quarter | Refusal | | | Released | Total |
|---|---|---|---|---|---|---|
| | | Counterfeit (suspected) | All other | Total | | |
| 2003–04 | **Total** | | *59 | 59 | N/A | N/A |
| 2004–05 | **Total** | | *68 | 68 | 96 | 164 |
| 2005–06 | **Total** | | *33 | 33 | 167 | 200 |
| 2006–07 | **Total** | | *59 | 59 | 77 | 136 |
| 2007–08 | **Total** | N/A | N/A | N/A | N/A | N/A |
| 2008–09 | **Total** | N/A | N/A | N/A | N/A | N/A |
| 2009–10 | Q1 | 0 | 2 | 2 | 0 | 2 |
| | Q2 | 6 | 2 | 8 | 9 | 17 |
| | Q3 | 0 | 12 | 12 | 31 | 43 |
| | Q4 | 3 | 5 | 8 | 37 | 45 |
| | **Total** | **9** | **21** | **30** | **77** | **107** |
| 2010–11 | Q1 | 0 | 22 | 22 | 38 | 60 |
| | Q2 | 0 | 16 | 16 | 27 | 43 |
| | Q3 | 0 | 18 | 18 | 39 | 57 |
| | Q4 | 0 | 12 | 12 | 27 | 39 |
| | **Total** | **0** | **68** | **68** | **131** | **199** |
| **2009–10 to 2010–11** | | **9** | **89** | **98** | **208** | **306** |

**Sources:** Inspectorate (2004, 2005b, 2006, 2007c, 2010d, 2011)
* Available reporting does not specify reasons for refusal.

**Table 21: Summary of National Chemical Residues Monitoring Program (NCRMP) results, FY 2005–06 to FY 2007–08**

| Source | Metric | Dairy | | | Eggs | | | Honey | | | Meat | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 2005–06 | 2006–07 | 2007–08 | 2005–06 | 2006–07 | 2007–08 | 2005–06 | 2006–07 | 2007–08 | 2005–06* | 2006–07 | 2007–08 |
| Domestic | # of tests conducted | 3,167 | 1,906 | 2,493 | 6,239 | 4,945 | 5,457 | 1,318 | 1,318 | 1,857 | N/A | N/A | 65,995 |
| | # residues detected | 12 | 12 | 9 | 63 | 158 | 136 | 42 | 44 | 50 | N/A | N/A | 1,132 |
| | % positive | 0.38% | 0.63% | 0.31% | 1.01% | 3.20% | 2.49% | 3.19% | 3.34% | 2.69% | N/A | N/A | 1.72% |
| | # violations detected | 12 | 3 | 8 | 63 | 155 | 25 | 42 | 6 | 1 | N/A | N/A | 335 |
| | **% compliant** | **99.62%** | **99.84%** | **99.73%** | **98.99%** | **96.87%** | **99.54%** | **96.81%** | **99.54%** | **99.95%** | **99.69%** | **N/A** | **99.49%** |
| Imported | # of tests conducted | 2,114 | 1,533 | 1,415 | 4,949 | 3,496 | 3,421 | 141 | 335 | 636 | N/A | N/A | 2,893 |
| | # residues detected | 8 | 24 | 28 | 27 | 33 | 33 | 2 | 10 | 30 | N/A | N/A | 7 |
| | % positive | 0.38% | 1.57% | 1.98% | 0.55% | 0.94% | 0.96% | 1.42% | 2.99% | 4.72% | N/A | N/A | 0.24% |
| | # violations detected | 8 | 3 | 22 | 27 | 33 | 14 | 2 | 9 | 5 | N/A | N/A | 1 |
| | **% compliant** | **99.62%** | **99.80%** | **98.45%** | **99.45%** | **99.06%** | **99.59%** | **98.58%** | **97.31%** | **99.21%** | **99.95%** | **N/A** | **99.97%** |
| Total | # of tests conducted | 5,281 | 3,439 | 4,358 | 11,188 | 8,441 | 8,878 | 1,459 | 1,653 | 2,493 | N/A | N/A | 68,888 |
| | # residues detected | 20 | 36 | 37 | 90 | 191 | 169 | 44 | 54 | 80 | N/A | N/A | 1,139 |
| | % positive | 0.38% | 1.05% | 0.85% | 0.80% | 2.26% | 1.90% | 3.02% | 3.27% | 3.21% | N/A | N/A | 1.65% |
| | # violations detected | 20 | 6 | 30 | 90 | 188 | 39 | 44 | 15 | 6 | N/A | N/A | 336 |
| | **% compliant** | **99.62%** | **99.83%** | **99.31%** | **99.20%** | **97.77%** | **99.56%** | **96.98%** | **99.09%** | **99.76%** | **N/A** | **N/A** | **99.51%** |

* Aggregate figures for meat and poultry products were not available for FY 2005–06.

**Sources:** CFIA (2006b, 2008a, 2011e)

**Table 22: Compliance rates of feed drug guarantee samples taken in commercial and on-farm feed mills**

| Fiscal year | Medicating Ingredients Guarantee Verification | | Drug Residue Contamination Inspection | |
|---|---|---|---|---|
| | % of samples compliant (commercial mills) | % of samples compliant (on-farm mills) | % of samples compliant (commercial mills) | % of samples compliant (on-farm mills) |
| 1991–92 | - | - | 72.6 | 72.7 |
| 1992–93 | - | - | 71.5 | 70.6 |
| 1993–94 | - | - | 81.6 | 76.7 |
| 1994–95 | - | - | 81.8 | 83.3 |
| 1995–96 | 76.2 | 51.9 | 76.4 | 78.8 |
| 1996–97 | 77.3 | 52.9 | 83.8 | 82.1 |
| 1997–98 | 77.7 | 53.8 | 83.1 | 85.9 |
| 1998–99 | 74.8 | 59.4 | 84.2 | 77.8 |
| 1999–00 | 80.6 | 60.2 | 82.7 | 87.5 |
| 2000–01 | 80.0 | 62.0 | 84.4 | 86.4 |
| 2001–02 | 79.0 | 41.9 | 85.3 | 83.6 |
| 2002–03 | 77.3 | 62.2 | 86.2 | 86.3 |
| 2003–04 | 79.9 | 56.8 | 90.3 | 79.0 |
| 2004–05 | 79.8 | 66.1 | 92.6 | 87.2 |
| 2005–06 | 78.2 | 61.1 | 92.5 | 90.1 |
| 2006–07 | 85.8 | 58.2 | 82.8 | 88.7 |
| **Average** | **78.2** | **58.2** | **81.9** | **80.8** |

**Sources:** CFIA (n.d.-a, n.d.-b)

**Table 23: Stakeholder organizations and committees consulted regularly by the VDD**

| Title | Description | Composition | Documented activities |
|---|---|---|---|
| CAHI | CAHI is an industry association representing companies that "develop, manufacture and distribute animal health products which include animal pharmaceuticals, biologics, feed additives and animal pesticides in Canada" (CAHI, 2012). Its mission is to "promote the timely availability of safe and efficacious animal health products that contribute to the health and welfare of animals, and a safe and productive food supply, both of which contribute to overall human health and well -being" (CAHI, 2012). | No list of members could be identified. | CAHI has consulted frequently with the VDD on a variety of issues of interest to its members. The documentation suggests it remains active in this capacity. |
| VDD Stakeholder Committee | The available documentation does not formally outline the mandate of the VDD Stakeholder Committee, although one document describes its purpose as "[providing] a forum for obtaining input from the stakeholder community on key issues that are the responsibility of the Veterinary Drugs Directorate" (HPFB, 2007b, p. 37). | The composition of the committee as of the last recorded stakeholder meeting in November 2006 is mentioned in the meeting summary report (VDD, 2006d). At this time, the Committee was composed of representation from producer groups, academia, veterinary associations, and other interest groups (e.g., Society for Environmentally Responsible Livestock Operation of Alberta, Canadian Environmental Network) (VDD, 2006d, p. 1). | There are records of nine VDD Stakeholder Committee meetings between 2002 and 2006, inclusive, as well as 17 communiqués; there is no evidence of Committee activity since around that time.<br>CAHPRAC, which was originally formed as a subcommittee of the Stakeholder Committee, appears to remain active. |

**Table 23: Stakeholder organizations and committees consulted regularly by the VDD**

| Title | Description | Composition | Documented activities |
|---|---|---|---|
| CAHPRAC | Formed as a subcommittee of the VDD Stakeholder Advisory Committee (VDD, 2008d, p. 8), CAHPRAC meets as required (Health Canada, 2010e, p. 6). | No list of members could be identified, but according to Health Canada, CAHPRAC consists of 17 members (Health Canada, 2010e, p. 6). | view of VDD performance reporting reveals that:<br>CAHPRAC was established by the VDD and the CFIA in association with CAHI in early 2008 (VDD, 2009b, p. 1).<br>CAHPRAC held its third meeting on June 26, 2008 (VDD, 2008d, p. 8).<br>A proposed approach to parallel review was presented at a CAHPRAC meeting in April 2010, suggesting the Committee remains active to the present (HPFB, 2010d, p. 10). |

**Table 24: Quantity of antimicrobials in dosage form distributed in Canada for use in animals, 2006–2008 (Canadian Animal Health Institute)**

| Antimicrobial class aggregation and importance in human medicine (1-4 scale, 1 being most important) | | Total active ingredients (kg) | | | % change, 2006-08 | % change, 2007-08 |
|---|---|---|---|---|---|---|
| | | 2006 | 2007 | 2008 | | |
| Aminoglycosides | *1–2 | 5,121.60 | 4,302.20 | 5,816.88 | 13.58% | 35.21% |
| Amphenicols | 3 | N/A | N/A | 3,242.03 | N/A | N/A |
| β-lactams (2006 and 2007) | 2 | 58,538.00 | 52,594.00 | N/A | N/A | N/A |
| β-lactams (2008) | 2 | N/A | N/A | 109,152.97 | N/A | N/A |
| Cephalosporins | 1–2 | 702.00 | 850.00 | N/A | N/A | N/A |
| Fluoroquinolones | 1 | 591.00 | 443.10 | 411.44 | -30.38% | -7.15% |
| Ionophores, chemical coccidiostats, and arsenicals (2006 and 2007) | 4 | 455,753.00 | 445,952.00 | N/A | N/A | N/A |
| Ionophores, chemical coccidiostats, arsenicals, and nitroimidazoles (2008) | ^4 | N/A | N/A | 472,384.36 | N/A | N/A |
| Lincosamides | 2 | 67,825.30 | 55,872.30 | 41,222.12 | -39.22% | -26.22% |
| Macrolides and pleuromutilins (2006 and 2007) | **2–3 | 136,496.50 | 118,724.80 | N/A | N/A | N/A |
| Macrolides, pleuromutilins, and bacitracins (2008) | **2–3 | N/A | N/A | 210,868.75 | N/A | N/A |
| Tetracyclines | 3 | 847,280.60 | 753,168.40 | 680,601.15 | -19.67% | -9.63% |
| Trimethoprim and sulfonamides | ^^2–3 | 50,789.00 | 38,961.00 | 59,165.54 | 16.49% | 51.86% |
| Other antimicrobials (2006 and 2007) | Various | 143,029.00 | 146,879.80 | N/A | N/A | N/A |
| Other antimicrobials (2008) | Various | N/A | N/A | 32,706.00 | N/A | N/A |
| **Total** | **N/A** | **1,766,126.00** | **1,617,747.60** | **1,615,571.23** | **-8.52%** | **-0.13%** |

***** These are designated Category 1 if used systematically, and Category 2 if used topically
^ Nitroimidazoles are banned in food animals, but would be considered Category 1.
** Until recently, pleuromutilins were intended only for topical use in humans and would have been considered Category 3; however, recent advances suggest systemic use may be possible, in which case they may be designated Category 1 or 2.
^^ Combination products (TMS) would be Category 2, but either group of drugs alone would be Category 3.

**Source:** PHAC (2011, pp. 81, 92)

**Notes:** Values do not include own-use imports or active pharmaceutical ingredients used in compounding. CAHI's 2008 data were provided to CIPARS under different aggregations of antimicrobial agents than previous years. "Other antimicrobials" include: clavulanic acid, bambermycin, ceftiofur, cephapirin, neomycin, nitrofurantoin, nitrofurazone, novobiocin, polymixin, sodium iodide, and virginiamycin.

**Table 25: Expert Advisory Committees (EACs) associated with the VDP**

| Title | Description | Composition | Documented activities |
|---|---|---|---|
| AC on Animal Uses of Antimicrobials and Impact on Resistance and Human Health | The goal of the Committee is "to provide information relevant to reducing the potential resistance and human health and safety impacts associated with animal uses of antimicrobial agents" (Health Canada, 2001b). | The Committee's composition is outlined in its final report (Advisory Committee on Animal Uses of Antimicrobials and Impact on Resistance and Human Health, 2002, p. 156). | • There are records of ten meetings of the Committee between 1999 and 2002 (Health Canada, 2004b).<br>• The Committee published a report in 2002, entitled "Antimicrobials in food animals in Canada: Impact on resistance and animal health" (Advisory Committee on Animal Uses of Antimicrobials and Impact on Resistance and Human Health, 2002; Prescott, 2002).<br>• There is no evidence of Committee activity since the publication of the 2002 report. |
| AC on MUMS (also known as MUMS & Aquaculture Committee) | Little information is available on the mandate or composition of this Committee. | No list of members could be identified. The available documentation states that the Committee was created to "provide on-going and timely advice to VDD as it develops policies to address the issue of MUMS" (VDD, 2005b, p. 5) noting that it will include representation from producers, veterinarians, drug manufacturers, and consumer/food safety groups. | • The Committee evolved from a working group established in May 2005 at the 6th VDD Stakeholder Committee Meeting (VDD, 2005b, p. 5); a draft ToR document was produced, but has not been provided by Health Canada.<br>• It is mentioned most recently in VDD performance reporting from Q4 FY 2008–09, in which the VDD planned to consult with the Committee on an updated MUMS definition and establish a list of MUMS drugs for small ruminants (VDD, 2009h). |
| EAC on Antimicrobial Resistance Risk Assessment | Founded in 2005 (VDD, 2007f), the Committee's focus is "to review scientific information and provide expert advice relevant to the assessment of risks and benefits of human and non-human uses of antimicrobial agents" (Antimicrobial Resistance Advisory Committee, 2004).<br>According to Health Canada,the Committee meets 2-3 times per year (Health Canada, 2010e). | Criteria guiding the selection of members are provided in the Draft ToRs (Antimicrobial Resistance Advisory Committee, 2004), but no membership list could be obtained. | • A draft ToR document was prepared in 2004 (Antimicrobial Resistance Advisory Committee, 2004).<br>• The Committee met four times between its founding in 2005 and winter 2007 (VDD, 2007f).<br>• VDD performance reporting mentions that a finalized antimicrobial risk categorization document was sent to the AMR Expert Advisory Committee members in December 2006 (it is assumed the document was referring to this Committee rather than the AC on Animal Uses of Antimicrobials and Impact on Resistance and Human Health) (VDD, 2006e, pp. 5–6). |
| EAC on Veterinary Natural Health Products (EAC-vNHP) | This Committee provides the HPFB with recommendations for developing regulations around veterinary natural health products (EAC-vNHP, n.d.; VDD, 2011b).<br>According to Health Canada, the EAC-vNHP meets 2-3 times a year (Health Canada, 2010e, p. 7). | The committee membership list is available on Health Canada's website (Health Canada, 2009). | • The first meeting of the EAC-vNHP was held in November 2008 (VDD, 2009b, p. 1).<br>• According to recent VDD performance reports, this Committee was active in 2009 (VDD, 2009i), and prepared a draft recommendation report in June 2010, with a final report due in July (VDD, 2010e).<br>• Meeting minutes posted on Health Canada's website show the EAC-vNHP was active at least as recently as May 2011 (Health Canada, 2011g). |
| Horse as a Food Producing Animal (HFPA AC) | Little information about this Committee is available. | No list of members could be identified. | • VDD performance reporting from FY 2008–09 states that "[VDD] can not commit significant human or financial resources to pursue the Horse as a food project until we establish a working definition for MUMS, a |

**Table 25: Expert Advisory Committees (EACs) associated with the VDP**

| Title | Description | Composition | Documented activities |
|---|---|---|---|
| | | | pilot for Aquaculture and Small ruminants such as sheep" (VDD, 2008e, p. 2).<br>• According to VDD performance reporting for FY 2009–10, work is underway on an initiative pertaining to the horse as a food-producing animal (VDD, 2009g, p. 4). |
| Own Use Importation (OUI) Task Force | The OUI Task Force was established by Health Canada in December 2006. The Task Force's final report was published for comments in December 2008, with a commenting period extending into March 2009 (Mathew, 2009). | Committee composition is outlined in its final report (available on Health Canada's website); while active, it included representatives from producer and consumer groups, veterinary associations, and provincial and federal governments, including the VDD, the Inspectorate, AAFC, DFAIT and the CFIA (OUI Task Force, 2008). | • The OUI Task Force is currently dormant (Health Canada, 2011b, p. 18) |
| VDD ELDU Advisory Committee | The available documentation does not formally outline the mandate of the ELDU Advisory Committee. | A 2004 Issue Identification Paper lists the Committee's members, which include representatives from industry, academia, veterinarians, and provincial and federal governments (ELDU Advisory Committee, 2004, p. 29) | • The ELDU Advisory Committee participated in the preparation of an Issue Identification Paper published in October (ELDU Advisory Committee, 2004, p. 29); this is the first reference to the Committee in the documentation available.<br>• A ToR document appears to have been developed for the Committee (VDD, 2009j), but this is no longer available on the Health Canada website (Health Canada, 2011d).<br>• A presentation to the Committee from May 2005 is included in the available documentation (Alexander, 2005).<br>• The Committee is mentioned most recently in VDD performance reporting from 2008, which mentions that a final ELDU policy had been sent to it (VDD, 2008f, p. 1). |
| VDD Science Issues Review Committee (SIRC) | According to the Terms of Reference, SIRC's mandate is to "ensure that veterinary drugs in the Canadian marketplace do not pose a threat to the health of Canadians and that they are safe and effective for animals" (SIRC, 2004, p. 2). SIRC is chaired by and reports to the DG, VDD, and is supported by a secretariat (2004, p. 3). It was originally expected to meet "on a regularly scheduled weekly basis" (2004, p. 4). | Information about membership is provided in the Committee ToRs, but no membership list appears to be available. | • Performance reporting refers to SIRC as early as mid-2003 (VDD, 2003e).<br>• A Terms of Reference (ToR) document was prepared in 2004 (SIRC, 2004).<br>• SIRC is mentioned as early as mid-2008 in documentation relating to progress with respect to MUMS (VDD, 2008e, p. 2). |

**Table 25: Expert Advisory Committees (EACs) associated with the VDP**

| Title | Description | Composition | Documented activities |
|---|---|---|---|
| Expert Advisory Panel on Aquaculture | The Expert Advisory Panel on Aquaculture is composed of experts in toxicology, fish science and aquaculture veterinarians from the provincial and federal sectors (VDD, 2007a). The Panel's objective is to explore key issues related to veterinary drugs in the context of aquaculture, and to "advise on potential mechanisms that will protect food safety, public health as well as the growing industry" (VDD, 2007a). | No list of members could be identified. | • The Panel was established in June 2006 (VDD, 2007a).<br>• Documentation shows the Panel met in June 2006 (VDD, 2006f, p. 1) and January 2007 (VDD, 2006e, p. 4, 2006g).<br>• A policy discussion document developed with the Panel's assistance was posted online for public consultation on March 23, 2007 (VDD, 2006e, p. 6).<br>• There is no mention of the Panel in available documentation since early 2007. |

**Table 26: HRAs completed by the VDD's HSD in response to requests by the CFIA**

| Date of CFIA request | Date of HRA | Subject of HRA | VDD conclusions and recommendations |
|---|---|---|---|
| January 30, 2007 | February 9, 2007 | Health risk assessment for cattle intended for slaughter that have been fed a mixture of medicating ingredients, some of which are not approved for cattle | Noted that there were many uncertainties related to the combination of various approved drugs at recommended and higher than recommended levels, as well as the presence of unapproved drugs in feed. As a result, the risks to human health from consumption of these cattle could not be predicted. The VDD therefore recommended that the exposed cattle (both finisher and grower) should not be slaughtered for human consumption for 50 days. |
| Unknown | April 17, 2007 | Potential risk to human health from consumption of milk and meat derived from cattle and sheep treated with copper sulphate that is contaminated with dioxins | Concluded that specified dioxin levels do not pose any significant risk to human health resulting from consumption of milk and meat derived from these animals. Recommended that the CFIA should inform the manufacturer and/or importers that Health Canada does not recommend usage of a non-DIN copper sulphate and the manufacturer of copper sulphate should be informed that they should contact the VDD for requirements for obtaining market authorization. |
| February 2007 | April 2007, 2007 | Potential risk to human health resulting from consumption of domestic and imported eggs which have been found to contain ionophore residues during 2004–2007 fiscal years. | Concluded that the health risk associated with the consumption of eggs contaminated with ionophore residues is not considered to be significant except for salinomycin. Recommended that the CFIA take appropriate actions to ensure that the cross contamination is eliminated at feed mills to minimize carry over of the drugs between the batches of feed for different species; ensure that there is no deliberate use of unapproved products, and consider improving the methodology for detecting these ionophores in feeds. |
| August 24, 2007 | September 13, 2007 | Health risk to human and animal health associated with antibiotic residues in ethanol byproducts (derived from fuel ethanol production) intended for livestock feeds | Concluded that levels of residues derived from ethanol byproduct feeds, if present in edible tissues of food animals, are expected to be very low and not likely to pose undue adverse health risk to humans and food animals. Identified potential safety concerns for horses fed with monensin-containing ethanol by-products and for tilapia fed with tylosin-containing ethanol by-products. Noted that further assessment required specific information on the levels of monensin to be used in ethanol production. Recommended that maximum inclusion rate of tylosin-containing distillers grain by-products in diet for tilapia should not exceed 30% on a dry matter basis. |
| January 2, 2008 | January 26, 2009 | Health risk associated with the potential residues of erythromycin in distillers' grain ethanol byproducts derived from fuel ethanol production and intended for livestock feeds | Concluded that levels of erythromyscin residues derived from ethanol byproduct feeds, if present in edible tissues of food animals, are expected to be very low and unlikely to pose adverse health risks ro humans or animals. |

**Sources:** (CFIA, 2007a, 2007b, 2008c; VDD, 2007e, 2007g, 2007h, 2007i, 2009k)

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