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FOOD AND DRUGS ACT

Regulations Amending the Food and Drug Regulations (Veterinary Drugs — Antimicrobial Resistance)

P.C. 2017-459 May 5, 2017

His Excellency the Governor General in Council, on the recommendation of the Minister of Health, pursuant to subsection 30(1) (see footnote a) of the *Food and Drugs Act* (see footnote b), makes the annexed *Regulations Amending the Food and Drug Regulations (Veterinary Drugs — Antimicrobial Resistance)*.

Regulations Amending the Food and Drug Regulations (Veterinary Drugs — Antimicrobial Resistance)

Amendments

1 Subsection C.01.001(1) of the *Food and Drug Regulations* (see footnote 1) is amended by adding the following in alphabetical order:

List A means the document, entitled *List of Certain Antimicrobial Active Pharmaceutical Ingredients*, that is published by the Government of Canada on its website, as amended from time to time; (*Liste A*)

List B means the document, entitled *List of Certain Veterinary Drugs Which May Be Imported But Not Sold*, that is published by the Government of Canada on its website, as amended from time to time; (*Liste B*)

List C means the document, entitled *Veterinary Health Products*, that is published by the Government of Canada on its website, as amended from time to time; (*Liste C*)

veterinary health product means any of the following drugs that is in dosage form and that is not manufactured, sold or represented for use in the diagnosis, treatment, mitigation or prevention of a disease, disorder or abnormal physical state, or its symptoms:

- **(a)** a substance set out in Column I of Part 1 of List C that is consistent with the descriptive information set out in Columns II to V, or any combination of any substances in which all the medicinal ingredients are substances set out in Column I of Part 1 of that list if that combination is, in respect of each of those substances, consistent with the descriptive information set out in Columns II and III and the descriptive information set out in Columns IV and V that is, within each of those columns, common to those substances;
- **(b)** a homeopathic medicine set out in Column I of Part 2 of List C that is consistent with the descriptive information set out in Columns II to V, or any combination of homeopathic

medicines set out in Column I of Part 2 of that list if that combination is, in respect of each of those homeopathic medicines, consistent with the descriptive information set out in Columns II and III and the descriptive information set out in Columns IV and V that is, within each of those columns, common to those homeopathic medicines; and

- **(c)** a traditional medicine set out in Column I of Part 3 of List C that is consistent with the descriptive information set out in Columns II to V, or any combination of traditional medicines set out in Column I of Part 3 of that list if that combination is, in respect of each of those traditional medicines, consistent with the descriptive information set out in Columns II and III and the descriptive information set out in Columns IV and V that is, within each of those columns, common to those traditional medicines; (*produit de santé animale*)

2 The Regulations are amended by adding the following after section C.01.013:

C.01.013.1 Section C.01.013 does not apply in respect of a veterinary health product.

3 The Regulations are amended by adding the following after section C.01.014.12:

C.01.014.13 Sections C.01.014 to C.01.014.7 do not apply in respect of a veterinary health product.

4 The Regulations are amended by adding the following after section C.01.018:

C.01.018.1 Section C.01.018 does not apply in respect of a veterinary health product.

5 The Regulations are amended by adding the following after section C.01.019:

C.01.019.1 Section C.01.019 does not apply in respect of a veterinary health product.

6 The Regulations are amended by adding the following after section C.01.611:

C.01.612 (1) Every manufacturer or importer who sells a veterinary drug in dosage form that contains an active pharmaceutical ingredient that is set out in List A, or every person who compounds such a drug, shall, in a form established by the Minister, submit to the Minister an annual report identifying for each drug, the total quantity sold or compounded and an estimate of the quantity sold or compounded for each intended animal species.

(2) The annual report described in subsection (1) is for a period of one calendar year and shall be submitted on or before March 31 of the year following the calendar year covered by the report, beginning with the first full calendar year after the day on which this section comes into force.

C.01.613 (1) No person shall import a drug into Canada for the purpose of administering it to an animal that produces food or an animal that is intended for consumption as food if the sale of the drug in Canada would constitute a violation of the Act or these Regulations.

(2) Subsection (1) does not apply to a drug that is described in List B.

C.01.614 (1) Sections 43 to 58 of the *Natural Health Products Regulations* apply in relation to a veterinary health product, as if that product were a *natural health product* as defined in subsection 1(1) of those Regulations.

(2) A veterinary health product shall display, on the principal display panel of the inner and outer label, the statement: “Veterinary Health Product / Produit de santé animale” or “Produit de santé animale / Veterinary Health Product”.

(3) Section C.01.600 and paragraph C.01.604(b) do not apply in respect of a veterinary health product.

C.01.615 (1) Every manufacturer or importer of a veterinary health product shall notify the Minister of the sale of that product in Canada at least 30 days before the day on which that sale is commenced.

(2) The notification shall be in a form established by the Minister and contain the following information:

- **(a)** the name, mailing address, telephone number and email address of the manufacturer or importer;
- **(b)** the brand name under which the veterinary health product is sold;
- **(c)** the pharmaceutical form in which the veterinary health product is sold;
- **(d)** the strength per dosage unit;
- **(e)** the route of administration;
- **(f)** a quantitative list of the medicinal ingredients and a qualitative list of the non-medicinal ingredients;
- **(g)** the species of animal for which the veterinary health product is recommended; and
- **(h)** the use or purpose for which the veterinary health product is recommended.

(3) A manufacturer or importer who has provided the Minister with a notification under subsection (1) shall provide the Minister with any changes to the information required under subsection (2), in a form established by the Minister, at least 30 days before the day on which the veterinary health product to which the changes relate is sold.

C.01.616 If the Minister has reasonable grounds to believe that a veterinary health product may no longer be safe, the Minister may request that the manufacturer or importer of the veterinary health product provide the Minister, within 15 days after the day on which the request is received, with information and documents demonstrating that the veterinary health product is safe.

C.01.617 (1) The Minister may direct the manufacturer or importer to stop the sale of a veterinary health product if

- **(a)** the manufacturer or importer does not, within the required period, provide the Minister with the information and documents requested under section C.01.616;
- **(b)** the information and documents provided by the manufacturer or importer in accordance with section C.01.616 do not demonstrate that the veterinary health product is safe; or
- **(c)** the Minister has reasonable grounds to believe that the sale of the veterinary health product would be a violation of the Act or these Regulations.

(2) The Minister shall lift a direction to stop the sale of a veterinary health product if the manufacturer or importer provides the Minister with information and documents demonstrating that

- **(a)** in the case of a direction to stop a sale under either paragraph (1)(a) or (b), the veterinary health product is safe;
- **(b)** in the case of a direction to stop a sale under paragraph 1(c), the sale of the veterinary health product would no longer be a violation of the Act or these Regulations; or
- **(c)** the situation giving rise to the direction to stop the sale of the veterinary health product did not exist.

7 Subsection C.01A.001(2) of the Regulations is replaced by the following:

(2) In this Division and in Division 2, *drug* does not include any of the following:

- **(a)** a dilute drug premix;
- **(b)** a *medicated feed* as defined in subsection 2(1) of the *Feeds Regulations, 1983*;
- **(c)** an active ingredient that is for veterinary use and that is not an active pharmaceutical ingredient;
- **(d)** an active pharmaceutical ingredient for veterinary use that is not required to be sold pursuant to a prescription and that is also a *natural health product* as defined in subsection 1(1) of the *Natural Health Products Regulations*;
- **(e)** a drug that is used only for the purposes of an experimental study in accordance with a certificate issued under section C.08.015.

8 (1) The portion of paragraph C.01A.002(1)(b) of the Regulations before subparagraph (i) is replaced by the following:

- **(b)** subject to subsection (3), importing or compounding, pursuant to a prescription, a drug that is not commercially available in Canada by one of the following persons:

(2) Section C.01A.002 of the Regulations is amended by adding the following after subsection (1):

(1.1) This Division and Division 2 do not apply to a veterinary health product or an active pharmaceutical ingredient that is used in the fabrication of a veterinary health product.

(3) Section C.01A.002 of the Regulations is amended by adding the following after subsection (2):

(3) This Division applies to the importing, by a pharmacist, a veterinary practitioner or a person who compounds a drug under the supervision of a veterinary practitioner, of an active pharmaceutical ingredient for veterinary use that is for the purpose of compounding, pursuant to a prescription, a drug in dosage form that is not commercially available in Canada, if that ingredient is set out in List A.

9 Table II to section C.01A.008 of the Regulations is amended by adding the following after item 6:

TABLE II

Item	Categories of Drugs
7	Active pharmaceutical ingredients set out in List A that are for veterinary use

10 Section C.08.001 of the Regulations is replaced by the following:

C.08.001 For the purposes of the Act and this Division, ***new drug*** means a drug, other than a veterinary health product,

- **(a)** that contains or consists of a substance, whether as an active or inactive ingredient, carrier, coating, excipient, menstruum or other component, that has not been sold as a drug in Canada for sufficient time and in sufficient quantity to establish in Canada the safety and effectiveness of that substance for use as a drug;
- **(b)** that is a combination of two or more drugs, with or without other ingredients, and that has not been sold in that combination or in the proportion in which those drugs are combined in that drug, for sufficient time and in sufficient quantity to establish in Canada the safety and effectiveness of that combination and proportion for use as a drug; or
- **(c)** with respect to which the manufacturer prescribes, recommends, proposes or claims a use as a drug, or a condition of use as a drug, including dosage, route of administration or duration of action, and that has not been sold for that use or condition of use in Canada for sufficient time and in sufficient quantity to establish in Canada the safety and effectiveness of that use or condition of use of that drug.

Transitional Provision

11 (1) In this section, *fabricate*, *package/label*, *import* and *active pharmaceutical ingredient* have the same meaning as in subsection C.01A.001(1) of the *Food and Drug Regulations*.

(2) Every person who, on or before the day on which section 7, subsections 8(1) and (3) and section 9 of these Regulations come into force, fabricates, packages/labels, tests or imports an active

pharmaceutical ingredient for veterinary use may continue to do so without an establishment licence if they submit an application for a licence under section C.01A.005 of the *Food and Drug Regulations* within 14 months after that day.

(3) Subsection (2) applies until the determination of the licence application is made under section C.01A.008 or C.01A.010 of the *Food and Drug Regulations*.

Coming into Force

12 (1) These Regulations, except section 7, subsections 8(1) and (3) and section 9, come into force on the 180th day after the day on which they are published in the *Canada Gazette*, Part II.

(2) Section 7, subsections 8(1) and (3) and section 9 come into force on the first anniversary of the day on which these Regulations are published in the *Canada Gazette*, Part II.

REGULATORY IMPACT ANALYSIS STATEMENT

(*This statement is not part of the regulations.*)

Executive summary

Issues: Antimicrobial resistance (AMR) is a serious and growing public health threat in Canada and around the world. As more microbes become resistant to antimicrobial drugs (or antimicrobials), these drugs become less effective in preventing and controlling infection. The overuse and misuse of antimicrobials in animals is a contributing factor to the development and spread of AMR. The development and spread of antimicrobial-resistant pathogens in animals can pose serious risks to human health when they are transmitted as food-borne or water-borne contaminants. Antimicrobial-resistant infections are associated with a greater risk of death, more complex illnesses, longer hospital stays and higher treatment costs. Based on available information, close to 80% of the total volume of antimicrobials sold in Canada are sold for use in animals. The *Food and Drug Regulations* (FDR) currently do not provide the necessary regulatory oversight of antimicrobials for veterinary use to mitigate the risk of AMR.

Description: Amendments to the FDR will improve the regulatory oversight of antimicrobials for veterinary use. The new regulations will require veterinary active pharmaceutical ingredients (APIs) imported or sold in Canada to be manufactured in accordance with good manufacturing practices (GMPs); require persons who import, fabricate, package, label or test veterinary APIs to do so in accordance with an establishment licence (EL); restrict the own use importation of unauthorized veterinary drugs; require manufacturers, importers and compounders of veterinary antimicrobials to provide sales volume information by species; and introduce an alternative, less burdensome pathway for manufacturers to legally import and sell certain low-risk veterinary drugs, known as veterinary health products (VHPs), that could reduce the need for antimicrobials.

Cost-benefit statement: The regulations are anticipated to cost industry and government $41.9 million net present value over 10 years. The quantified costs relate to new GMP and EL requirements that

would be levied against persons who import, fabricate, package, label or test veterinary APIs; a requirement to submit sales volume and species data of antimicrobials sold in Canada; and costs to Health Canada relating to new compliance and enforcement activities. The non-quantifiable benefits of the proposed regulations include domestic and international consumer confidence in the livestock and poultry sectors; a reduction of the incidence of antimicrobial-resistant bacteria; a reduction in environmental residues of antimicrobials; and the introduction of alternative products through the new pathway for VHPs.

"One-for-One" Rule and small business lens: Both the "One-for-One" Rule and the small business lens apply to the proposed amendments. The anticipated administrative burden on businesses required to report on sales volume and species sales data is estimated to be $253,011 (constant 2012 dollars) per year, or $633 per company. The small business lens would apply and was considered for the following stakeholder groups: food animal producers, veterinarians, compounding pharmacists, and entities manufacturing or importing VHPs. Veterinarians and pharmacists were identified as saving a significant amount in administrative costs. However, those who wish to compound and manufacture antimicrobials will be required to comply with new associated GMP and EL costs.

Domestic and international coordination and cooperation: The proposed amendments to the FDR are designed to enhance the regulatory alignment of the Department of Health (the Department) with the United States and the European Union.

Background

Antimicrobials

An antimicrobial is a drug that can destroy micro-organisms, including those that can cause disease, or inhibit their growth. In Canada, more than three quarters of antimicrobials are sold for use in animals. (see footnote 2) Of those, approximately 90% are used to promote growth or to guard against disease and infection. Globally, the use of antimicrobials in food-producing animals continues to rise, from just over 63 000 tons in 2010 and to well over 100 000 tons (projected) by 2030. (see footnote 3) In Canada alone, it is estimated that 1.6 million kilograms of antimicrobials were distributed for animal use in 2013. (see footnote 4)

Antimicrobial resistance

Antimicrobial resistance (AMR) is a serious and growing public health threat in Canada and around the world. (see footnote 5) Antimicrobials, such as antivirals, antibiotics, antifungals and antiparasitics, kill most micro-organisms (i.e. viruses, bacteria, fungi and parasites, respectively) or slow their growth. However, those micro-organisms with greater resistance survive and continue to infect their host. AMR is the ability of micro-organisms to resist the effects of antimicrobials. The micro-organisms change in a way that reduces or eliminates the effectiveness of drugs designed to cure or prevent infections and/or disease caused by these micro-organisms. Micro-organisms may be naturally resistant or insensitive to antimicrobials, or may become resistant after being exposed to these drugs. Overuse and misuse of

antimicrobials, as well as the use of sub-potent antimicrobials resulting from inadequate quality controls, are the main contributors to the development of AMR. (see footnote 6)

Antimicrobial-resistant infections are associated with a greater risk of death, more complex illnesses, longer hospital stays and higher treatment costs. Recent reports (see footnote 7) (see footnote 8) have shown that infections caused by antimicrobial-resistant bacteria cause at least 2 million illnesses and at least 23 000 deaths annually in the United States. In Europe, about 25 000 patients die each year from drug-resistant bacterial infections. At a global level, deaths attributable to AMR are currently estimated to be 700 000 annually, and could reach up to 10 million by 2050, potentially costing world economies up to US$100 trillion.

Furthermore, the development of AMR has consequences not only for human health, but also for animal health. A reduction in the number of effective antimicrobials available to treat animal diseases can lead to increased animal suffering, higher death rates and, subsequently, economic losses to food animal producers and higher consumer food prices.

Antimicrobial use in animals and antimicrobial resistance

The development of antimicrobial-resistant pathogens in animals can pose serious risks to human health when they are transmitted as food-borne or water-borne contaminants. Furthermore, the overuse and misuse of antimicrobials in animals has helped to accelerate the resistance of micro-organisms to these drugs.

For example, between 2003 and 2011, the Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) tested 26 428 *Salmonella* samples from humans exposed to contaminated food products. (see footnote 9) Of these, 28% of the *Salmonella* strains were resistant to one or more antimicrobials. In 2011, CIPARS observed consistently high levels of resistance to a specific antimicrobial, ceftiofur, in *Salmonella* isolates found in retail chicken products, as well as in *Salmonella* causing human infections. (see footnote 10) This antimicrobial resistance was attributed to the use of antimicrobials in chicken hatcheries. Once the use of that particular antimicrobial ceased, a significant decrease in antibiotic-resistant *Salmonella* was seen in both retail chicken and humans. (see footnote 11)

Domestic and international context

The World Health Organization (WHO) has long recognized the risks to human health resulting from the extensive use of antimicrobials in food-producing animals. The WHO considers that two of the key essentials in combating the development of AMR are assurance of the quality of the drug (i.e. good manufacturing practices [GMPs]) and measures to control the misuse of these drugs. (see footnote 12)

Internationally, regulatory agencies around the world have recognized the dangers of AMR and are taking steps to reduce its occurrence. For example, the United States announced in 2014 a National Strategy for Combatting Anti-Microbial Resistant Bacteria. The U.S. Food and Drug Administration (U.S. FDA) has followed up on this by introducing measures to encourage a more prudent use of antimicrobials in food-producing animals, including the removal of growth promotion claims, requiring

greater veterinary oversight and compelling manufacturers to provide data respecting the volume of sales and an estimate of how the products are used. Unlike Canada, the United States and other jurisdictions, including those of the European Union, do not allow the importation of unapproved veterinary drugs for a person's own use (such as the direct administration to food-producing animals) and require that active pharmaceutical ingredients (APIs) used in the manufacture of veterinary drugs be compliant with GMPs.

In Canada, veterinary drugs in dosage form that are authorized for sale have to meet strict standards, including the requirement to be manufactured according to GMPs. Manufacturing in accordance with GMPs lowers the risk that a drug may be contaminated or adulterated with substances that may cause harm to human or animal health. GMPs also ensure that a drug contains the medicinal ingredient in the quantities necessary to achieve the desired clinical effect. For example, GMPs can reduce the risk of sub-potent antimicrobials entering the market, and thus decrease the possibility of AMR developing from exposure to these drugs. Veterinary drugs in the form of APIs are currently not required to meet GMPs.

However, in the spring of 2015, the Auditor General of Canada released a report on AMR. The Auditor General found that "Health Canada has not taken some important steps needed to promote prudent antimicrobial use in food animals. For example, the Department has not strengthened existing regulations to prohibit farmers from importing unlicensed non-prescription antimicrobials that are important to human medicine for use in their own animals." (see footnote 13)

In response, on April 18, 2015, Health Canada issued a notice of intent in the *Canada Gazette*, Part I, informing stakeholders and the public of the Department's intent to propose amendments to the FDR that will begin to address AMR, including increasing controls at the border.

In October 2015, the president of the Public Health Agency of Canada joined the other G7 health ministers in signing the Berlin Declaration on Antimicrobial Resistance, thereby acknowledging that the emergence of AMR is an increasing global health threat, and committed to pooling national efforts to promote the prudent use of antimicrobials and combat AMR.

Issues

In Canada and around the world, fewer antimicrobials remain effective in preventing and controlling infection as more microbes become resistant in both human and animal settings. The current regulatory oversight of antimicrobials for veterinary use under the FDR does not adequately address the risks to human health. The following are some key areas of concern.

Lack of quality standards for veterinary APIs

Manufacturing in accordance with GMPs can reduce the risk that a drug may be contaminated or adulterated. APIs used in the manufacture of veterinary drugs are currently not required to be compliant with GMPs, as is the case for APIs used in the manufacture of human drugs. This means that the quality of veterinary APIs is less certain and cannot be easily verified. This increases the likelihood that sub-potent APIs or those contaminated with harmful impurities may be introduced into veterinary

drugs. If either of these things occurs, it may pose a risk to both animal and human health, both from direct exposure to harmful substances, including as residues in human food, or through the development of antimicrobial-resistant strains of disease causing pathogens introduced into the food supply.

In Canada, establishments that fabricate, package, label, distribute, import, wholesale, or test a drug (with some exceptions, including APIs for veterinary use) must do so in accordance with an EL issued under Part C, Division 1A, of the FDR. The licence application, approval and renewal process allows for the inspection by Health Canada of establishments and processes as a means of confirming compliance with GMP requirements.

Ability for persons to import unauthorized veterinary drugs for own use in food-producing animals

Many antimicrobials that are important to treat humans are freely available for use in animals without veterinary oversight. They may be imported to Canada as APIs or in dosage form without any regulatory oversight, if the importation is not made for the purposes of sale; this is also known as "own use importation" (OUI). This lack of regulatory oversight allows food animal producers to import large quantities of unapproved drugs, and enables these producers to administer such drugs to entire herds.

These drugs have not been authorized for sale in Canada, and consequently, they have not been subject to scientific scrutiny by Health Canada. Although many of these drugs may have been authorized for sale in other jurisdictions, their unregulated use in Canadian food-producing animals can pose a risk to human and animal health. For example, inadequate direction respecting the withdrawal period of a drug could result in higher and potentially unsafe levels of drug residues in the human food supply, and antimicrobials that are not supported by adequate instructions for use or are sub-potent could lead to the development and spread of AMR.

Furthermore, as a substantial number of veterinary APIs can be directly administered to animals without the need to be formulated into a dosage form, some food animal producers may directly import these drugs for use in their business. This activity is driven by economic factors. APIs are less expensive than an authorized drug in dosage form (i.e. a drug that has been issued a drug identification number [DIN] by Health Canada) and are typically available from foreign manufacturers at prices lower than those in Canada. This practice can pose a risk to human and animal health for a number of reasons. APIs imported in this manner are not subject to regulatory oversight; therefore, there are no requirements for labelling the API with instructions for use, reporting adverse drug reactions or recalling an unsafe API — requirements that promote the safe and effective use of a drug.

Lack of information regarding the volume of veterinary antimicrobials sold to facilitate surveillance, prevention and control of AMR

In order to combat the development and spread of AMR, it is important to know at an early stage where resistance is developing and in what species. This type of surveillance is expensive and time-consuming as it involves laboratory analysis of samples, and limited resources may be better focused if geographical areas or species at higher risk were identified and targeted for enhanced surveillance. Sales volume data

would be an important tool in maximizing the efficiency of current surveillance programs, as efforts could be focused on more heavily used drugs. Having improved data could also support Health Canada's ongoing efforts to encourage the prudent use of antimicrobials in food-producing animals. For example, if sales volume data indicates a heavy use of an antimicrobial in a particular species, this could be correlated with resistance information in bacteria of human health importance to determine the need for measures to mitigate risk. Currently, the FDR do not require the reporting of sales volume data.

Restrictive regulatory pathways creating barriers for the availability of approved low-risk health management tools to reduce the need for veterinary antimicrobials

Many low-risk veterinary drugs (also referred to as veterinary health products [VHPs]), which could be used as additional tools for managing the health of animals and could potentially reduce the need to use antimicrobials, have not been authorized for sale in Canada. This is mainly because of the difficulty manufacturers have in generating sufficient scientific data respecting the safety and efficacy of the drug to meet the existing regulatory requirements for a "new drug" (which would require the filing of a new drug submission as per Division 8 of the FDR). Other than the "in human" aspect, many of these drugs meet the definition of a *natural health product* under the *Natural Health Products Regulations* (NHPR) and have been approved for sale for use in humans under those regulations. (see footnote 14) However, natural health products for veterinary use continue to be regulated under the more restrictive and burdensome requirements of the FDR.

To provide oversight and facilitate the sale of these types of drugs, the Department has, since 2012, put in place a voluntary non-regulatory pilot program known as the Interim Notification Pilot Program (INPP). The INPP provides Health Canada with a mechanism for determining whether products are likely to pose a risk to health. (see footnote 15) However, the Program is only applicable to low-risk products used in non-food-producing animals, and has the added limitation of being unsupported in regulation. The INPP currently benefits from the use of a list of substances that have been evaluated by Health Canada as safe for use in these types of products. (see footnote 16)

The only other means available for these drugs to be approved for sale is through the Veterinary Drugs Directorate Emergency Drug Release (EDR) program. (see footnote 17) Regulatory authority for EDR is provided by sections C.08.010 and C.08.011 of the FDR, which state that the sale of a drug made under these sections is exempt from all other provisions of the *Food and Drugs Act* and the FDR. This means that unlike other authorizations, Health Canada has no ability to gather information about the drug or to take actions that could mitigate risks associated with its use. Veterinarians must make an application through the EDR program on an individual basis and the authorization only allows for a small quantity of drugs (in effect, a veterinarian would have to file an EDR application each time he or she wanted to prescribe the drug). This results in a time-consuming and inefficient process both for veterinarians and Health Canada. An example of drugs that continue to be requested through the EDR program are certain calcium supplements that are used in lactating dairy cattle to help maintain calcium levels, so as to reduce the incidence of disease and, subsequently, the need for antimicrobial therapy. These drugs have been the subject of hundreds of individual requests by veterinarians through this program.

Objectives

The overall objective of this proposal is to limit risks to human health by reducing the likelihood of resistance to antimicrobials in humans as a result of the improved regulatory oversight of antimicrobials sold for veterinary purposes.

More specifically, the proposed regulatory amendments are intended to

- require veterinary APIs imported or sold in Canada to be manufactured in accordance with GMPs;
- require persons who fabricate, package and label, import or test an API for veterinary use to do so in accordance with an EL;
- restrict the own use importation of certain unauthorized drugs (including APIs);
- require manufacturers and importers to provide sales volume information by species for veterinary antimicrobials; and
- introduce an alternative, more appropriate pathway for manufacturers to legally import and sell low-risk VHPs.

Description

Ensuring the quality of APIs for veterinary use

Similar to the existing provisions for human use APIs, the new regulations would require persons who fabricate, package, label, import or test an API for veterinary use to do so in accordance with an EL. These requirements will also be applied to any person (including veterinarians and pharmacists) who import for the purpose of compounding an antimicrobial for veterinary use that is set out on List A (to be incorporated by reference into the FDR). (see footnote 18) Antimicrobials set out on List A are those that Health Canada has deemed to be important in human medicine, and for which the development of AMR could have an impact on human health. In addition, the regulations will prohibit the import or sale of veterinary APIs that are not manufactured according to GMPs as currently set out in Part C, Division 2, of the FDR. APIs for veterinary use that meet the definition of *natural health product* in subsection 1(1) of the NHPR would be exempted from these requirements. This will align regulatory oversight for natural health products for veterinary use with that for human use.

Controlling the own use importation of veterinary drugs

Regulatory amendments are needed to eliminate the use of antimicrobials in the form of APIs in food animals and to restrict the use of unauthorized drugs in food animals. Amendments will incorporate by reference into Division 1 of the FDR a list of veterinary drugs (List B (see footnote 19)) that may be imported (but not sold) in Canada despite not being authorized for sale by Health Canada.

The regulations will also prohibit the importation of a drug for the purpose of administering it to an animal that produces food or an animal that is intended for consumption, if its sale would contravene the *Food and Drugs Act* or regulations, unless the drug is set out in List B. In effect, this would mean that food animal producers will no longer be able to import unauthorized drugs for their own use, other than those drugs that appear on List B. Drugs on List B will be identified by manufacturer, brand name, dosage form, strength and country in which the product has been authorized for sale.

Health Canada is making publicly available helpful and user-friendly support materials that elaborate on the processes for List B and what information the Minister will consider before adding a drug to List B. This information includes the following: evidence that demonstrates the comparability with a drug that has been authorized for sale in Canada, including the dosage form and strength, the route of administration, the existence of a maximum residue limit in the specified species and food commodity; whether the labelled conditions of use fall within the directions for use of the comparable Canadian approved drug; whether the drug is in final dosage form; whether the drug has been approved for sale in a recognized foreign jurisdiction that has a drug approval system comparable to that of Canada; and whether the drug is a medicated premix.

Drugs that contain medically important antimicrobial APIs on List A and prescription drugs will not be considered for inclusion on List B.

Gathering information that supports AMR surveillance

The new regulations will require manufacturers and importers who sell a veterinary drug in dosage form that contains an ingredient on List A and every person who compounds such a drug to provide an annual report to the Minister of Health. The report will identify for each API on List A the total quantity sold or compounded and an estimate of the quantity sold or compounded for each intended animal species.

The information is intended to be correlated against resistance patterns in conducting evidence-based AMR risk analysis. This new provision aims to address the lack of information on the type and volume of veterinary APIs that are being imported or used in Canada. Surveillance would fill existing gaps on antimicrobial sales volume information related not only to antimicrobials being sold and distributed via existing regulated routes but also imported veterinary drugs and APIs.

Facilitating access to VHPs

The new amendments create a pathway to allow for the importation and sale of VHPs (for use in both food-producing animals and companion animals) distinct from the existing drug approval pathways in Part C, Divisions 1 and 8, of the FDR.

Amendments will incorporate by reference into Division 1 a list of VHPs (List C (see footnote 20)). A *veterinary health product* will be defined in regulation as a drug in dosage form described on List C that is not manufactured, sold or represented for use in the diagnosis, treatment, mitigation or prevention of the disease, disorder or abnormal physical state, or its symptoms. In other words, products making general health claims, such as promoting or maintaining organic functions or the health

of an animal, will be considered to be VHPs. Prescription drugs and drugs containing ingredients on List A will not be considered for inclusion on List C. A guidance document indicating the criteria the Minister will consider when amending List C will be made publicly available.

Manufacturers or importers of a VHP will be exempted from Part C, Division 1, related to Assignment and Cancellation of Drug Identification Numbers (C.01.014 to C.01.014.7), Part C, Division 1A (Establishment Licences), and Part C, Division 2 (Good Manufacturing Practices). In addition, the definition of *new drug* in Part C, Division 8, of the FDR has been amended to exclude VHPs, thereby exempting them from all provisions in Division 8. Manufacturers and importers of VHPs will not be required to obtain DINs or be required to hold an EL. However, GMP requirements of the NHPR apply to these products, and manufacturers and importers will be required to notify the Department at least 30 days before commencing the sale of a VHP. Although not required by regulation, it is Health Canada's intent to verify that each VHP has been correctly notified.

The new regulations allow the Minister to require the manufacturer or importer of a VHP to provide information if there are reasonable grounds to believe the VHP is no longer safe. The Minister will be able to stop the sale of a VHP if no information is provided, the information provided is insufficient, or the sale of the VHP represents a contravention of the *Food and Drugs Act* or the FDR. The Minister will be able lift a direction to stop sale if the information provided in response to the request is sufficient, the situation giving rise to the stop sale did not exist, or the situation giving rise to the stop sale has been corrected.

Additionally, the statement "Veterinary Health Product / Produit de santé animale" will be required on the label.

Consequential amendments and changes requested by the Standing Joint Committee for the Scrutiny of Regulations

Amendments to the *Establishment Licensing Fees (Veterinary Drugs) Regulations* will exempt veterinary APIs from fees associated with the examination of an application for an EL or the amendment of an EL — or the annual review of an EL — that deal exclusively with veterinary APIs. The Department intends to introduce a fee for the examination of an EL application in respect of veterinary APIs under a subsequent proposal and, in doing so, will comply with the requirements set out in the *User Fees Act*. Pursuing a fee structure for EL examination at a future date allows the Department time to gather a more accurate estimate of the costs associated with this activity and to better align with a future fees structure for the examination of an EL for human APIs (also currently exempted from fees).

The Department will also be taking this opportunity to address a recommendation made by the Standing Joint Committee for the Scrutiny of Regulations (SJCSR) by correcting the French text of the remission provision in the *Establishment Licensing Fees (Veterinary Drugs) Regulations*. This amendment will better align the text with the English version by removing an inconsistency in terminology. Specifically, the French text in subsection 11(1) is revised to replace the existing reference to "cette somme" with the more appropriate term "ce montant." The words "une somme" are already used in subsection 11(1) to refer to a different amount, which leads to confusion as to which amount is being referred to.

Regulatory and non-regulatory options considered

The Department has assessed regulatory and non-regulatory options (detailed below), taking into consideration regulatory divergence across provinces and territories, alignment with international regulatory partners, consistency with international standards, level of impact on innovation and competitiveness, as well as appropriate level of oversight.

Option 1: Status quo

For the reasons previously discussed, the status quo does not represent a viable means of achieving the Department's public health mission and objectives regarding AMR. It would not restrict the uncontrolled importation of unauthorized veterinary drugs for a person's own use, provide a means of gathering data to support AMR surveillance activities, ensure the quality of veterinary APIs or allow for the legal sale of VHPs and the expansion of their use to food-producing animals.

In addition, the Canadian regulatory framework for veterinary drugs would continue to be inconsistent with the international standards and practices of its trading partners.

Option 2: Non-regulatory initiatives

Under this option, the existing regulatory framework for veterinary drugs would have continued as is under the previous regulations (status quo) with a view to implementing the policy objectives of the regulatory proposal through voluntary means. This option was rejected for several reasons.

Ensuring the quality of APIs for veterinary use

Manufacturing drugs in accordance with GMPs represents a substantive ongoing investment on the part of an API manufacturer. Although many globally based veterinary API manufacturers may already be compliant with GMPs, this is presumed mainly to be a result of more stringent laws already in place in many foreign jurisdictions, including the United States and the European Union. Due to financial considerations, it is unlikely that all manufacturers would voluntarily agree to meeting GMPs. In addition, under a voluntary scenario, Health Canada would be unable to monitor manufacturers to ensure they are compliant with GMPs and take effective action if they are found to be out of compliance.

Controlling the own use importation of veterinary drugs

Consideration was given to establishing a non-regulatory list of unauthorized veterinary drugs (similar to the proposed List B) that Health Canada considered as safe for use in food-producing animals. Health Canada could also be more proactive in educating food animal producers about the risks associated with the use of unauthorized drugs. Although some producers may have chosen to follow Health Canada recommendations, it would be difficult to convince all producers of the risks associated with using products not authorized for sale in Canada when these same products are available on the market in other jurisdictions. Producers that may have been using unauthorized products with good effect may not see the harm in continuing their use. In addition, as the main driver for own use importation is

economic, it was presumed that many producers would continue to accept the risks associated with using an unauthorized drug.

Gathering information that supports AMR surveillance

Although gross sales volume data is available through public sources, the level of detail available from this information means that it is of limited use to support AMR surveillance activities. Although consideration was given to requesting more detailed information such as estimates of sales volume by species from manufacturers, importers and compounders of veterinary antimicrobials, the response was not anticipated to be high for a number of reasons, including the administrative burden (although small) that it would place on persons to gather the information and the assumption that many manufacturers may consider this type of information to be confidential and may therefore be reluctant to disclose it voluntarily.

Facilitating access to VHPs

The INPP was intended as a short-term pilot to test the feasibility of an alternate means of providing access to veterinary health products. The program has proven to be successful in that over 600 VHPs have been brought to market under it. This has allowed Health Canada to provide a level of safety oversight to these products as well as gather information about the type of drugs that are being sold and the manufacturers that are active in this field. It has also allowed Health Canada to monitor somewhat the safety of these products through adverse drug reaction reporting, the results of which indicate, as expected, that these products do indeed represent a low level of risk when used appropriately. However, as the sale of the drugs under this program continues to contravene the FDR (specifically subsection C.01.014(1), which prohibits the sale of a drug unless a DIN has been assigned) and as manufacturers have been advocating for the expansion of the program to include food-producing animals, the continuation of the program was considered untenable without a basis in law.

Option 3: Amending the FDR — Selected option

This option will amend the FDR to ensure veterinary APIs imported or sold in Canada are manufactured in accordance with GMPs, restrict the own use importation of certain unauthorized drugs, require manufacturers to provide sales volume information by species for veterinary antimicrobials and facilitate access to VHPs.

This option was chosen because it represents the most efficient and effective approach for improving the oversight of antimicrobials for veterinary use. The regulations will be supported by non-regulatory mechanisms, such as guidance, and collaborative approaches with federal, provincial and territorial partners, industry and other stakeholders that have a role to play in mitigating the risk of AMR associated with antimicrobial use in food-producing animals. This option is preferable because it will result in a more coherent and balanced approach to risk management without imposing an undue burden on stakeholders.

In selecting this option, the Department will achieve the stated objective, within its mandate, of reducing the risks to human health associated with the use of antimicrobials in animals. This option was developed in consultation with stakeholders and takes into account international standards.

A number of variations on the proposed regulatory option were considered. With respect to APIs, consideration was given to applying only the GMP component without the requirement for ELs. It was felt that this would not provide the desired level of oversight and assurance of the quality of APIs and could negatively impact the ability of Canadian manufacturers to export APIs to other jurisdictions where a licensing scheme and inspection component are part of their drug laws.

An import permit system requiring farmers to apply for a permit to import drugs for their own use was considered. However, it was felt that in comparison to the proposal supported by List B, a permit system would impose an unnecessary administrative burden on farmers wishing to import drugs for their own use and would require additional government resources for its administration without providing any additional safety benefit.

For VHPs, consideration was given to having a pre-market application and DIN assignment process similar to what already exists for veterinary drugs in Divisions 1 and 8 of the FDR, which would also allow for the provision of information to support efficacy claims but not to the standard required for a new drug submission under Division 8. It was felt that defining a VHP so as to limit the claims that a manufacturer could make would alleviate the need to conduct a pre-market review of supporting data. Not requiring manufacturers and importers of VHPs to file a pre-market application and wait for a decision from Health Canada allows them to come on market quicker and reduces their administrative burden.

Benefits and costs

The cost-benefit analysis focuses on the administrative, compliance and government costs as a result of the regulations surrounding the federal oversight of antimicrobials. The benefits were determined to be non-quantifiable and are described qualitatively.

Cost-benefit statement

Quantified impacts (CAN$, 2016 price level / constant dollars)				
	Base Year (Year 1)	**Final Year (Year 10)**	**Total (Net Present Value)**	**An Av**
Costs				
Industry: Veterinary and Pharmacist GMP, incl. EL application	$6,179,920	$3,929,920	$29,646,645	$4,

Update of EL — API manufacturers	$3,000,000	$0	$3,000,000	$3
Administrative reporting (sales volume and species)	$295,680	$295,680	$2,222,103	$2
VHP notification	$30,464	$30,464	$228,944	$3
VHP label cost (one time)	393,875	$0	$393,875	$3
Costs to Government	$173,272	$852,146	$6,362,985	$8
Total costs	**$10,073,211**	**$5,108,210**	**$41,854,552**	**$5,**

Qualitative impacts (non-quantifiable)

Benefits

- Reduction in the overall use of antimicrobials.
- Reduction in health care costs due to antimicrobial-resistant infection.
- Longevity of existing pool of front-line antimicrobials for human and animal use.
- Reduced probability of prescribing antimicrobials of last-resort and high-risk.
- Limiting antimicrobial residue in the environment.
- Better control of veterinary medicines entering Canada.
- Potential to increase passive disease surveillance by veterinarians.
- Increased consumer confidence in Canadian meat and poultry products both domestically and internationally.
- Alignment with international jurisdictions.
- Alternative pathway for VHPs to enter the marketplace.
- May present new opportunities for Canadian business to develop alternatives to antimicrobials.

Costs

- Price differential between Canadian and U.S. prices for branded veterinary pharmaceuticals.
- Potential increase in time required for appropriate veterinary oversight.
- Access to antimicrobials could be reduced, potentially affecting livestock and poultry mortality.
- Potential increase in veterinary costs to producers.

- Potential increase of on-farm costs due to decrease in accessibility of antimicrobials.

The total net present value costs of the regulations are anticipated to be $41.9 million over 10 years or $5.7 million a year. These costs reflect new EL and GMP requirements for veterinarians and pharmacists who compound or import antimicrobials that are not marketed in Canada, as well as new administrative reporting requirements for manufacturers, importers and compounders of antimicrobials. Anticipated benefits include a reduction in the overall use of antimicrobials, a reduction in environmental residues of antimicrobials, and increased consumer confidence in Canadian meat and poultry products.

The full cost-benefit analysis is available upon request.

Costs

Similar regulations are currently in place for human APIs. While there is some recognition that both human and veterinary APIs are sourced from the same suppliers, the costing assumes that these suppliers are separate and unique entities.

Industry

Industry costs include three main components: the implementation of GMPs for persons involved in the importation, fabrication, packaging, labelling or testing of veterinary APIs and associated EL costs; the administrative reporting of sales volume and species data by manufacturers, importers and compounders of veterinary antimicrobials on an annual basis to Health Canada; and the administrative costs for manufacturers and importers of VHPs to notify Health Canada when commencing sale of a VHP.

In consultation with veterinarians and pharmacists represented by their respective associations, Health Canada estimated that approximately 75 veterinarians and pharmacists would continue to import or compound antimicrobials. The regulations would make it mandatory for veterinarians and pharmacists who wish to conduct these activities in accordance with an EL and GMP requirements. A further 100 API manufacturers are anticipated to provide an EL application and are assumed to already be compliant with GMPs, in accordance with the regulations. Using a conservative estimate for GMP and EL costs, it was estimated that these activities would cost approximately $52,000 per year, as well as an initial ramping up cost of $30,000 in the first year of the regulations coming into force for GMPs. An additional $440 would be required for each veterinarian wishing to compound or manufacture an API in order to submit a yearly EL application. Total costs for year one are estimated to be $82,000 and ongoing costs from Year 2 onwards are anticipated to be $52,000 per business. The total compliance burden is estimated to be $32.7 million in net present value over 10 years or $4.5 million annually for all businesses. The total administrative burden is anticipated to be $224,856 in net present value over 10 years or $29,920 annually.

A new administrative reporting requirement is included in the regulations, which stipulates that manufacturers, importers and persons who compound drugs included on List A for veterinary use will be required to submit their sales volume and species data to Health Canada annually. It is assumed that this

submission would be done electronically as a means of reducing reporting costs for both industry and the Government. Based on the results of a 2015–2016 stakeholder costing survey and information from the Drug Product Database, Health Canada estimates that approximately 264 companies would be required to submit this data. These companies include manufacturers of branded antimicrobials, wholesalers and API manufacturers and importers. Using U.S. FDA estimates and previous work at Health Canada on reporting requirements, it was estimated that these activities would take approximately 10 hours and have a resource cost per hour of approximately $112. The net present value of these activities over 10 years is estimated to be $2.2 million or approximately $295,680 per year.

Manufacturers and importers of VHPs will be required to notify Health Canada at least 30 days before commencing sale of their products in Canada. It is estimated that it would take approximately two hours to complete a standard notification form.

In addition, VHP manufacturers who are already marketing their products in Canada under the INPP will be required to amend their labels in compliance with the regulations. Assuming that there are currently 685 products being marketed under the INPP and an initial, one-time cost of $575 per label in order to comply with the VHP regulations, the cost of amending existing labels is estimated to be approximately $393,875 and will occur in year one.

The total cost of VHP compliance and administrative activities is anticipated to be $622,819 in net present value over 10 years or approximately $69,852 annually.

Canadian farmers of food-producing animals

Although the regulations will increase controls over the availability of antimicrobial APIs, data indicating the quantity of APIs being directly used in food-producing animals was not readily available and as a result the impact on farmers was difficult to quantify.

In situations where farmers import products through OUI, there could be a minimal increase in costs for drugs until they are added to List B, as farmers would only be able to purchase these drugs in Canada. However, many respondents to the 2015 costing survey indicated that OUI becomes less attractive as the Canadian dollar becomes weaker relative to foreign currencies.

Due to significant reductions in the availability of inexpensive antimicrobial APIs, there could be some increased risk that farmers who are currently relying on these unauthorized drugs may see an increase in the percentage of food animals lost to disease. However, not having ready access to APIs may encourage farmers to replace these with authorized drugs through consultation with veterinarians to determine appropriate, safe and effective replacements.

Evidence from Sweden, Denmark and the Netherlands, where a ban on the dispensing of prophylactic antimicrobials was instituted, indicated an initial small reduction in animal weight and an increase in death following the coming into force of their regulations. (see footnote 21) As a result, farmers in these countries experienced a small fall in revenues, which returned to pre-regulation levels within two years due to changes in animal husbandry, such as providing more space for animals, using antimicrobial

alternatives, ensuring appropriate therapeutic use of antimicrobials, and engaging in more robust cleaning protocols.

The regulations do not represent as dramatic a change as the ban instituted in those European countries; the relative costs are therefore expected to be less.

Government

Costs to Government include compliance and enforcement activities to be carried out by Health Canada. It is estimated that approximately 6.25 full-time equivalent employees will need to be allocated on an ongoing basis for border, compliance verification, establishment licensing and billing, and enforcement of GMP activities. Costs to Government are variable over the first five years following the regulations coming into force, with an estimated ongoing annual cost of $852,146. Total cost to Government over 10 years in net present value is estimated to be $6.4 million.

There will be approximately $306,250 per year in foregone revenues to Health Canada from the collection of establishment licence fees (associated with GMPs), as a result of the exemption to the *Establishment Licensing Fees (Veterinary Drugs) Regulations*.

Own use importation and price differential

Canadian farmers can currently import veterinary products for their own use. The rationale behind this OUI was twofold: a small number of products that farmers require for their livestock and poultry may not be available for sale in Canada, and many products could be obtained at a lower cost when sourced from outside the country.

When the new restrictions on OUI were proposed, there was some concern that Canadian farmers of food-producing animals would be adversely affected due to the current availability of certain products only in foreign jurisdictions and the generally higher price differential of Canadian products. Accurate quantitative data regarding the extent of OUI was not readily available, and no respondent to the 2015 costing survey indicated that they were engaged in OUI of antimicrobials. In addition, the large associations representing food animal producers indicated that this was not an activity that they encourage. They did, however, indicate that the majority of products imported through OUI include ivermectins (anti-parasitic medication for intestinal worms, lice and mites), magnesium-sulfate boluses (predominately used in feedlots as a digestive or laxative), veterinary natural health products, and vaccines (such as autogenously killed vaccines for *Salmonella* and *Adenovirus*).

It was difficult to obtain an accurate estimate of the price differential of antimicrobials between Canada and the United States. An Ipsos Reid study estimated the value of importation for own use, including APIs, at around $50M. A 2007 International Federation for Animal Health (IFAH) survey also estimated that branded drug manufacturer members in Canada lost approximately $120 million in potential sales. Some survey respondents indicated that costs could be up to five times higher in Canada than in the United States for some products, while another respondent indicated that the price for injectable products was closer to 15–25% higher in Canada. In late 2015, the low Canadian dollar relative to the

American dollar disincentivized importation for own use, making this a less attractive practice for food animal producers to engage in.

The regulations could present a small increase in cost for farmers who participate in OUI. However, due to the types of products being imported through this mechanism and the lack of responses indicating that antimicrobials were being imported, costs and impacts on farmers were determined to be negligible.

Canadian consumers of meat and poultry products

Any costs passed to the consumer would be for changes in feed costs, and potential losses of livestock or poultry.

Canadian consumers should not see increases in meat and poultry product costs due to the regulations. Evidence from jurisdictions where bans on antimicrobials in food-producing animals were instituted demonstrated no change in the price of poultry and small increases in the cost of beef and pork (i.e. $2.08 per pig or less than $0.02/lb). As the regulations do not ban antimicrobials in food-producing animals, it is assumed that costs would be negligible or zero.

Benefits

The benefits of the regulations are non-quantifiable as the evidence between reducing AMR in animals and its full impact on human health is not well established. While there are isolated reports and documentation describing human health being impacted by animal health, broad conclusions regarding the quantifiable impacts of the regulations cannot be established.

A number of causal and consequential links that have been made regarding the future benefits of the regulations are described below.

It is assumed that the regulations could lead to overall human and animal health improvements over the longer term through improvements in oversight on the supply and quality of antimicrobials dispensed to food-producing animals.

Consumer confidence in the Canadian livestock and poultry market

Consumer confidence in Canadian livestock and poultry sectors is an important determining factor for the financial success of domestic producers.

Canada has a large beef and pork export market of approximately $6 billion, the majority of which is exported to the United States. The livestock and poultry industries are vulnerable to the effects of AMR due to its potential to affect animals at a farm or feedlot and the strong competition from competing exporters of similar meat and poultry products (i.e. Brazilian beef, Chilean seafood, and Danish pork), which could lead to reduced consumer confidence in Canadian food products. Canadian farmers of food-producing animals represent a nearly $58 billion per year industry or an average per farm receipt of $727,000.

If Canada had not proceeded with proposed policies to address AMR and come into greater alignment with international standards for use of antimicrobials in food animals, there may have been potential implications on trade. For example, an importing country (i.e. the European Union, the United States or Japan) could have started requiring "certification" that the food of animal origin was raised and produced using international standards. The World Trade Organization has already ruled that restrictive trade practices on Canadian livestock producers and processors by the United States has led to lost revenues of approximately $1.06 billion per year; the potential damage from restrictive trade due to an on-farm AMR outbreak could be devastating for the Canadian market.

Not responding to the potential consequences of AMR could have presented economic challenges. A recent report from G7 health ministers stated that current rates of AMR may cause a gross domestic product contraction in Organisation for Economic Co-operation and Development countries equal to 0.03% in 2020, 0.07% in 2030, and 0.16% in 2050. This would result in cumulative losses of approximately US$2.9 trillion.

By ensuring better alignment with international jurisdictions and addressing gaps that allow the direct use of veterinary APIs in food-producing animals, the regulations should remove a significant economic risk.

Reduced incidence of multi-drug resistant bacteria

The incidence of AMR in food-producing animals could have direct consequences for human health and Canadian industry. It is assumed that the regulations will reduce the chances of serious AMR outbreaks through the implementation of strict quality as well as import controls over veterinary APIs.

A disease outbreak caused by multi-drug resistant bacteria could shut down an entire industry. For example, a multi-drug resistant outbreak of *Aeromonas salmonicida* closed a fish hatchery in New Brunswick in 2004 due to fears of the bacteria spreading to other locations and no known available antimicrobial being successful. Total losses due to fish depopulation amounted to $1.15 million and an additional $68,000 was required to fully clean the hatchery.

Further, the link between AMR in animals leading to sickness in humans has been well documented. Food-producing animals represent a significant reservoir of AMR since approximately one third of bacteria that affect animals can affect humans. Interaction with food products which may have come into contact with antimicrobials is high whether it is in the surrounding environment or in the food that Canadians consume. There has been evidence that supports resistant strains of *E. coli*, *Campylobacter* and *Salmonella* bacteria (see footnote 22) seen in food-producing animals, later infecting humans.

Improvement in AMR surveillance activities

The establishment of a surveillance framework is a vital tool in mitigating and tracking AMR in Canada. Currently, information about the amount of antimicrobials being dispensed to food-producing animals and which species are receiving these products is limited. It is anticipated that the regulations will

produce new data which can be forwarded to CIPARS to align with AMR action plan commitments and activities.

Surveillance frameworks are important public health tools that can effectively identify patterns of risk. As a result of the contribution to the existing framework established by CIPARS, the potential for on-farm outbreaks could be reduced by improving predictive AMR modelling and augmenting the knowledge base within the Health portfolio.

While this provision is not anticipated to directly impact human health, there could be the potential for new activities which could benefit Canadians, such as demographic information relating to where AMR risk management actions can be focused, directed correspondence to stakeholders (i.e. medical practitioners, veterinarians, farmers), or faster response/quarantine times in order to reduce the probability of a resistant microbe spreading elsewhere.

Reduced regulatory compliance costs for VHPs

The IFAH has estimated the average cost associated with developing a new veterinary drug at $250 million and can take place over a period of 6 to 12 years. This high financial and sustained resource cost represents a significant barrier to potential entrants into the Canadian market. Under the existing FDR, the manufacturer of a new veterinary drug would have to provide evidence of the safety and effectiveness of the drug through the filing of a new drug submission (NDS) to Health Canada. These requirements have been identified as being cost prohibitive for manufacturers and importers of VHPs, making it difficult to sell their products in Canada.

Health Canada has allowed some of these products to be approved for sale under the Emergency Drug Release (EDR) program; however, each EDR application must be reviewed individually, on a case-by-case basis, for the release of a single batch of drug to an individual veterinary. This process does not provide an efficient means to access drugs. In response, the INPP was introduced to allow VHPs to access the Canadian market.

Using figures from the INPP, approximately 685 products have been granted access through this mechanism across 136 companies. Assuming each of these products is a new veterinary drug that would require evidence of safety and effectiveness to satisfy the existing requirements for an NDS, the average cost to bring these products to market would be approximately $1.26 billion per VHP manufacturer.

There are a number of benefits of the regulations for VHPs. It will enable manufacturers of VHPs to enter the Canadian market at substantially reduced costs, including costs associated with developing a new veterinary drug as well as regulatory costs associated with seeking market authorization. The VHP pathway presents a new market opportunity for small-scale manufacturers, as well as potentially reduces the need to use antimicrobials by allowing access to alternatives.

“One-for-One” Rule

The amendments would initiate new reporting requirements for veterinary manufacturers, importers and compounders who sell antimicrobials; therefore, the “One-for-One” Rule would apply.

Under the new regulations, manufacturers, importers and compounders of veterinary antimicrobials will be required to submit sales volume and species data to Health Canada. It is assumed that this data will be submitted electronically as a means of reducing the overall paper and submission burden for reporting entities and Health Canada. There will also be a requirement for manufacturers, importers and compounders of eligible VHPs to notify Health Canada electronically when they intend to sell these products in Canada.

It was estimated that reporting on the volume and species of an antimicrobial would take approximately 10 hours per manufacturer, importer and compounder, at an hourly rate of $112. Approximately 264 entities would be required to report this administrative data to the Department for an annual administrative cost of $295,680.

Due to the relatively short time requirement to notify the Department of the sale of a VHP, it was estimated that two hours would be required per VHP manufacturer or importer at $112 per hour. The two-hour average estimate intends to capture manufacturers and importers with multiple and single product lines. Approximately 136 manufacturers were identified as being registered with INPP and are anticipated to notify Health Canada at an annual notification cost of $30,464.

Veterinarians and pharmacists who wish to import antimicrobials would be responsible for submitting an EL application on a yearly basis to Health Canada. The average salary of a veterinarian and pharmacist is $44 per hour and these activities are anticipated to take approximately 10 hours annually. This cost would only apply after Year 2 of the regulations due to the initial ramping up compliance costs of $30,000 in Year 1, which is assumed to include the EL application cost and GMP compliance costs. Total costs are anticipated to be $224,856 net present value over 10 years or approximately $29,920 per year for all importing veterinarians and pharmacists.

In total, the amendments would represent an increase in administrative costs (IN) of approximately $253,011 in constant 2012 dollars or an average cost of $633 per reporting entity.

Current initiative is an *IN*

Total annualized average administrative costs (constant 2012 $)	$253,011
Annualized average administrative costs (constant 2012 $)	$633

Small business lens

The small business lens applies to any regulatory proposals that impacts small business and has a nationwide cost impact of over $1 million annually. The Treasury Board Secretariat defines a small

business as any business, including its affiliates, that has fewer than 100 employees or between $30,000 and $5 million in annual gross revenues.

Four groups of small businesses were identified as being potentially impacted by the regulations: food animal producers, veterinarians, compounding pharmacists, and entities manufacturing or importing VHPs.

In designing these regulations, a number of means to minimize the impact on small businesses were identified and incorporated, as follows.

Importation for own use

Although food animal producers will no longer be able to import veterinary drugs for their own use, other than those on a list established by Health Canada (List B), the Department will consider adding to that list any drug that does not pose undue safety concerns. Antimicrobials would not be eligible to be included on the list; however, Canada's 79 668 farmers would continue to be able to access high quality pharmaceuticals from Canadian suppliers.

Access to VHPs

Improved access for Canadian farmers to a growing number of products that may improve or maintain the health of their animals may diminish the incidence of disease and thereby reduce the need for expensive therapeutic treatments. Furthermore, VHPs that are currently accessed through the EDR will now be freely available without veterinarian intervention.

Opportunities through reduced development costs for VHP manufacturers

VHP manufacturers will no longer have to generate the information required in a new drug submission to support a market authorization from Health Canada. A total of 136 manufacturers producing 685 products are currently marketing under the INPP, 111 of which would be defined as small businesses. The regulations will require that VHP manufacturers notify Health Canada when they intend to sell their products. While the full development costs of a veterinary branded drug product, inclusive of discovery and supporting evidence, could be upwards of $250 million, it is estimated that compliance and regulatory costs for VHP products will be approximately $799 per manufacturer.

Reduction in new fees for veterinarians and pharmacists

The regulations include a provision that all antimicrobials sales be reported to Health Canada by volume and species. There were concerns expressed by veterinarians that the proposed provision could add a significant amount of administrative burden in order to report on all antimicrobials that they dispense. Based on January 2016 estimates, this could impact 1 307 veterinarians and 40 704 licensed pharmacists; leading to potential reporting costs of $47,052,320 for all veterinary businesses per year. In order to reduce costs to veterinarians, they will be exempt from this requirement unless they import antimicrobials.

There were approximately 75 veterinarians and pharmacists that were identified through consultations as potentially importing antimicrobials for use in compounding activities. Under the regulations, they would be required to comply with GMPs as well as to file an EL application. GMP compliance is estimated to cost approximately $52,000 per company, and to cost an additional $30,000 in Year 1 to ramp up new compliance activities. Using estimates from the human API framework, the cost of an EL application is anticipated to be $4,300 per company. Veterinarians would be required to file an application for an EL and renew the EL annually. This activity was estimated to cost each veterinarian $440 annually.

As a means of reducing the new compliance burden levied on veterinarians and pharmacists who import antimicrobial APIs for the purpose of compounding, an exemption from the EL requirements was considered as a flexible option. The costing analysis is demonstrated below.

Regulatory flexibility analysis statement

	Initial Option		Flexible Option	
Short description				
Number of small businesses impacted	75		75	
	Annualized Average ($)	Present Value ($)	Annualized Average ($)	Present Value ($)
Compliance costs Annual cost of GMP activities EL Fee (see footnote 23)	 $4,154,920 $515,250	 $29,646,645 $3,872,223	 $4,154,920 N/A	 $29,646,645 N/A
Administrative costs	$29,920	$224,856	N/A	N/A
Total costs (all small businesses)	$4,700,090	$33,743,724	$4,154,920	$29,646,645
Total cost per small business	$62,668	$449,916	$55,399	$395,289
Risk considerations	• Some additional cost levied to veterinarians and pharmacists who would		• Low quality and uninspected API co entering the Canadian market, as ir	

	also face new GMP compliance costs.	activities would not occur.

The initial option has been selected in order to adequately assure the quality of veterinary APIs. It was considered that this could be best achieved through an EL application and establishment inspection process at little added cost to regulated parties, which will consist primarily of the administrative costs associated with preparing and filing an EL application.

Consultation

Since 2006, the Department has conducted engagement activities and various consultations in support of the modernization of the regulatory framework for veterinary drugs. Some of the key topics consulted on include the following: own use importation of unapproved drugs, importation and GMP requirements for veterinary APIs and reducing regulatory burden for low risk veterinary drugs. This proposal builds on the feedback received during those consultations, as well as incorporates international best practices. A summary of the consultations and feedback received is found below.

Overall, stakeholders have generally agreed with the issue, objective and key principles of the proposals to provide greater oversight of veterinary antimicrobials.

When considering whether the proposals can be effectively implemented, stakeholders have noted the importance of having a level playing field, a consistent regulatory approach and international alignment, notably with the U.S. FDA due to the integrated nature of the North American agri-food and veterinary drug markets. Discussions regarding implementation and transition planning have suggested a stepwise approach based on risk management and supported by education and awareness activities.

Task Force on Own-Use Importation (2006–2008)

The Task Force on Own-Use Importation was struck by the Department in December 2006 and membership consisted of food producer associations, the Canadian Animal Health Institute, consumer and veterinary associations, as well as provincial veterinary bodies and government representatives.

The mandate of the Task Force was to examine a new, more restricted approach to the own use importation of veterinary drugs. The Task Force final report was published in August 2008. (see footnote 24) The report made three recommendations:

- (1) That a voluntary Restricted Import Permit Program (RIPP) be created as a pilot project to determine program feasibility;
- (2) That a subcommittee be established in the fall of 2008 with the mandate of negotiating details of the RIPP for implementation by Health Canada; and
- (3) That regulatory reform in the area of veterinary drugs and biologics be recognized as essential to ensure timely availability and access to products that benefit livestock and Canadian producers and that support innovation and the development of new animal health technologies by the animal health sector.

In developing this regulatory proposal, the recommendation of the Task Force to establish an import permit system was further examined. It was felt that in comparison with the proposal supported by List B, a permit system would impose an unnecessary administrative burden on farmers wishing to import drugs for their own use as well as requiring additional government resources for administration.

Technical discussions on veterinary drugs regulatory modernization (January and March 2013)

These sessions (see footnote 25) included a broad range of stakeholders, representing the perspective of the veterinary pharmaceutical industry, food producer associations, veterinary associations, academics, as well as provincial and federal agriculture and public health officials.

These technical discussions covered a broad variety of topics related to the modernization of veterinary drug regulations, and an overall risk-based approach to drug approval, notably based on best international practices.

The proposals relating to importation of veterinary drugs for own use and importation of APIs generated support from stakeholders for enhanced regulatory oversight of these practices and introduction of an internationally recognized GMP- and EL-based quality standard for APIs. The main concern noted was the need for sufficient oversight on importation of APIs while aligning internationally.

Overall, feedback on the risk-based approach for regulating low-risk veterinary health products was positive, with support for the continuation of the INPP for Low Risk Veterinary Health Products that had been implemented in March 2012. The main concern noted was about a timely expansion of this program to include food-producing animal products.

Technical discussion session and bilateral consultations on increasing stewardship of medically important antimicrobials used in veterinary medicine (March 2015–July 2015)

The Department held consultations with a broad range of stakeholders, representing the perspective of the veterinary pharmaceutical industry, food producer associations, veterinary associations, as well as provincial and federal agriculture and public health officials, on the topic of increasing stewardship of veterinary antimicrobials, including proposals for increased regulatory oversight.

The scope of the consultation was on a series of interrelated regulatory and non-regulatory proposals that support each other towards better stewardship of medically important antimicrobials. The feedback pertaining to the proposed regulatory amendments is summarized as follows:

- Stakeholders expressed support for increased oversight on importation of veterinary drugs for own use and of APIs. As in 2013, stakeholders expressed support for these two proposals, and notably the need for requirement of GMPs as well as an EL for the importation of APIs. Concerns were expressed regarding the scope of application of the EL requirements for importation of APIs. For own use importation, there was overall support, with comments on the need to ensure that the competitiveness of the food-producing industry would not be affected, as well as to ensure that there are no concerns about some products that figure on the eligible products list.

- Low Risk Veterinary Health Products — Further to the voluntary INPP for companion animals, stakeholders have shown solid support and interest for the Department to expand this program to food-producing animals.
- Use information collection — Over the years, various stakeholders have highlighted gaps in the collection of accurate antimicrobial use information to compare with the resistance surveillance data.

2015 notice of intent

On April 18, 2015, Health Canada issued a notice of intent in the *Canada Gazette*, Part I, informing stakeholders and the public of the Department's intent to propose amendments to the FDR that will begin to address AMR, including increasing controls at the border. The Department received comments from two stakeholders who suggested that pharmacists who compound antimicrobials for veterinary use also be required to obtain an EL. Additionally, these stakeholders recommended that the Department take steps to eliminate the use of APIs in food-producing animals. The regulatory amendments being proposed to control OUI, as well as a non-regulatory initiative to ensure that all antimicrobial drugs for veterinary use (that are medically important in human use) are listed on the prescription drug list, should effectively eliminate the ability of food animal producers to use antimicrobial APIs directly in food-producing animals. Health Canada considered a requirement for compounding pharmacists to obtain an EL, but did not for the following reasons. Unlike veterinarians and physicians, pharmacists can and do compound drugs for both animals and humans. There is also no simple means of distinguishing APIs intended for human use from those intended for veterinary use. Although it was recognized that compounding pharmacists could still import APIs without an EL, the proposed regulations would still require that imported APIs be compliant with GMPs. Additionally, as substantive evidence of the quantities of antimicrobials currently being compounded and sold by pharmacists for food-producing animals was not readily available, it was not possible to determine the true extent of this practice and its potential impact on AMR. The proposed regulations, which would allow Health Canada to collect sales volume and species data from compounders, would allow for a reassessment of this practice in the future.

2015 costing survey

A number of targeted stakeholders were solicited for their input on the anticipated costs associated with key elements of the proposed regulations. Respondents included veterinary associations, livestock and poultry associations and drug manufacturer associations. Results of the survey were used to inform the costing estimates. Stakeholders did not voice concerns about the proposals, but rather emphasized the need to keep the administrative reporting costs as low as possible, such as providing a simple electronic means of reporting.

Prepublication in the *Canada Gazette*, Part I

The proposed *Regulations Amending the Food and Drug Regulations (Veterinary Drugs — Antimicrobial Resistance)* were prepublished in the *Canada Gazette*, Part I, on July 2, 2016, for comment for a 75-day

period. Over the course of the consultation period, Health Canada received hundreds of comments from 48 different respondents. Respondents included veterinary drug industry associations, food animal producers and associations, associations representing veterinarians, other federal government agencies, provincial ministries of health or agriculture veterinary drug sellers and importers and individuals.

Overall, respondents were supportive of measures to reduce the likelihood of resistance to antimicrobials in humans as a result of the use of antimicrobials for veterinary purposes. A number of comments were received that were outside of the scope of these regulations and are not considered here.

Ensuring the quality of APIs for veterinary use

All respondents indicated support for the proposal to increase regulatory oversight of veterinary APIs. Additionally, a significant number of respondents including food animal producers and associations, associations representing veterinarians, other federal government agencies and provincial regulators indicated that pharmacists who could import a List A drug for the purpose of compounding should not be excluded from the requirement to obtain an EL for this type of importation. Health Canada had considered this prior to prepublication but did not at the time perceive that the gap in regulatory oversight would represent a significant risk to human or animal health. This was mainly because information available to Health Canada indicated that only a few compounding pharmacies had imported very small quantities of drugs on List A in recent years and that this represented a relatively small part of their business activities. However, there remains the possibility for this gap in oversight to be exploited as other avenues currently available through which poor quality API can be imported are closed off. Therefore, the regulations will reflect the extension of the EL requirement to pharmacists, who import a veterinary drug on List A for the purpose of compounding. It is anticipated that few, if any, compounding pharmacies will seek to acquire an EL solely for the purpose of importing veterinary drugs on List A and will instead rely on Canadian-based suppliers.

A number of respondents suggested that Health Canada consider a ban on the use of APIs in food-producing animals. At the federal level, the Governor in Council has the authority to make regulations respecting the “sale” of a drug whereas how a drug is “used” generally falls within the practice of medicine. Although a regulation could have been proposed that would have prohibited the sale of an API for a specific use, these types of rules are considered to be difficult to enforce in practice and could limit the flexibility of veterinary practitioners in providing treatment options. Thus, Health Canada is of the opinion that the new regulations provide an appropriate level of oversight while still allowing the use of APIs for therapeutic reasons.

In light of comments received regarding the 6-month transition period regarding the EL applications, Health Canada has determined that a longer period of time would be required to evaluate the expected number of new EL applications. As a result, the transitional provision that allows a person to continue activities provided that they have filed an application for an EL has been extended to 14 months. Additionally, the coming into force for those regulations that are applicable to the GMP and EL

requirements for veterinary APIs has been extended to 12 months to allow manufacturers sufficient time to adjust to the new requirements.

Controlling the own use importation of veterinary drugs

Most respondents expressed support for the proposed measures to control own use importation. It was noteworthy that many of the associations representing food animal producers indicated that their existing guidance recommended against own use importation of veterinary drugs.

A number of respondents, including many associations representing food animal producers, indicated that they would like to be involved in populating List B prior to publication of the regulations in the *Canada Gazette*, Part II. Health Canada has developed a process for managing List B and has already begun to consider requests to add items to the list.

A number of respondents felt that some veterinary drugs for minor uses in minor species (MUMS) will no longer be available following the coming into force of the regulations and that the criteria which Health Canada will consider will preclude these drugs from ever being included on List B. The regulations supporting List B have been designed to allow Health Canada flexibility in deciding which drugs to place on List B weighing the need for them against the risks they may present, regardless of their MUMS status. Health Canada is aware of the challenges posed to bring drugs for MUMS to market and has been working with the pharmaceutical industry and other stakeholders to find ways to satisfy the existing regulatory requirements. For example, Health Canada is working on a separate and dedicated MUMS initiative, in collaboration with Agriculture and Agri-Food Canada (AAFC), to facilitate access to MUMS products and, in the last three years, five products for minor species have been authorized under this program.

A number of respondents, including one veterinary association, and several provincial regulators suggested that the restrictions pertaining to own use importation should be extended to companion animals. This was considered, but rejected, as Health Canada considered that allowing this practice to continue would impose negligible risks to human health.

A number of suggestions were received regarding the criteria that the Minister would consider when amending List B. These included holding consultations with provincial and territorial veterinary associations. Health Canada may consult directly with scientific experts, manufacturers and others, including veterinary associations, but does not expect that this would normally be necessary when amending List B.

Some respondents suggested that drugs should not be allowed on List B if the foreign drug is indicated for use in species that do not appear on the Canadian authorized equivalent. Health Canada will, in each case, conduct a thorough review of the foreign labelling in comparison to the Canadian approved product and will not add any drug to List B that would increase risks associated with its use over that of the Canadian product.

One respondent representing veterinary drug manufacturers suggested that importers of drugs on List B be required to notify of recalls and adverse drug reactions. As drugs on List B cannot be sold in Canada but must only be used by the person that imports the drugs, a recall, or removal from the marketplace, would not be applicable in this context. Health Canada, if it becomes aware of a foreign recall of a drug on List B, will take steps to publicly notify Canadians of the recall. With respect to adverse drug reaction (ADR) reporting, the Canada Vigilance system already provides a means for Canadians to report ADRs directly to Health Canada and it was felt that this provided a sufficient means of gathering this type of information.

Several respondents representing provincial regulators again indicated that an import-permitting scheme would provide greater oversight of own use importation. There are advantages to such a scheme, for example to gain information about the quantities of List B drugs being imported and by having contact information that could allow for direct notification of foreign recalls or other risks associated with the use of the drug. However, Health Canada felt that this would not provide significant additional risk management value beyond the evaluation it would conduct prior to adding a drug to List B and would present an additional burden on importers.

Gathering information that supports AMR surveillance

Some respondents representing provincial regulators and veterinary associations indicated that additional data such as the geographic location of sales or distribution should be reported. Health Canada recognizes that, in many instances, it may be difficult for a manufacturer or importer to know with certainty where a drug has been sold once it enters the distribution chain and, as such, did not wish to recommend extending the reporting requirements. Health Canada will have forms that will aid regulated parties to comply with the new regulations, which will allow them to provide additional details respecting the distribution of those sales if available.

Some respondents representing food animal producers commented that it would be difficult to know with certainty in which species a drug was used if it was indicated for multiple species. Health Canada believes that manufacturers and importers through their marketing activities should have a relatively good understanding of how their drug is used on the market and that compounders should have this information available to them from details included on a veterinary prescription. Therefore, in most instances, it should be possible to estimate the percentage of drug sold by species.

Finally, Health Canada has reconsidered the requirement to provide an annual report of sales volume data within a month after the end of the reporting period and believes that this would not allow sufficient time for a comprehensive and accurate report to be prepared. As the information in the reports will be used in part to plan AMR surveillance activities, it was considered more important that the report be complete and of high quality. Therefore, an additional two months (for a total of three months) will be allowed for the submission of the report to the Minister.

Facilitating access to VHPs

Respondents who commented on the VHP scheme expressed support for this initiative.

One respondent representing a provincial regulator suggested that VHP manufacturers be required to report any adverse drug reactions as opposed to only serious ADRs. This was rejected as it would establish a reporting threshold beyond that of higher risk drugs.

A number of respondents, including associations representing food animal producers, noted that as VHPs would not be issued a DIN, the current wording of the *Feeds Regulations* would prohibit their addition to animal feed. Health Canada is continuing to work with the Canadian Food Inspection Agency (CFIA) to identify the VHPs that would be acceptable for addition to animal feed and the means by which this could be accomplished.

A number of respondents, including veterinary drug sellers and importers, requested that Health Canada continue the practice from the current INPP program of issuing a Notification Number (currently, this is done by a third party under a pilot project scheme). Although not in regulation, Health Canada will operationally continue this practice and will issue a unique identifier to each VHP that is acceptably notified. Health Canada has also reconsidered the timing of the notification, and the regulations were therefore amended so that manufacturers and importers will have to notify the Minister of their intent to sell a VHP in Canada at least 30 days before the sale occurs. This will allow Health Canada the time necessary to verify that the drug is a VHP as defined in the regulations and that the notification is complete. The regulations were also amended to clarify that the VHP manufacturer or importer would have to re-notify if any changes were made to the information provided in the original notification at least 30 days before making the change.

Consequential amendments and changes requested by the Standing Joint Committee for the Scrutiny of Regulations

There were no comments directly related to the amendments to the *Establishment Licensing Fees (Veterinary Drugs) Regulations* or the amendments requested by the Committee.

Further consultation following prepublication

In the fall of 2016, the two main associations representing pharmacists and pharmacy regulators in Canada were apprised of the EL requirement being extended to pharmacists. Both associations responded favourably. A costing survey was also forwarded to them in November 2016, which was disseminated to their members. Responses from the survey were used to finalize the cost-benefit analysis supporting these regulations.

Summary of changes to the Regulations following prepublication

The regulations differ from those prepublished in the *Canada Gazette*, Part I, in the following manner:

- The definition of “veterinary health product” was revised to clarify that a veterinary health product is a drug in dosage form.
- Proposed subsection C.01A.002(3) was revised such that both pharmacists and veterinarians who import a veterinary drug on List A for the purpose of compounding a drug not commercially

available in Canada will be required to do so pursuant to an EL to reduce the possibility that poor quality APIs will be used in compounded drugs.

- Section C.01A.002 of the FDR was amended to clarify that Divisions 1A and 2 do not apply to veterinary health products or an active ingredient used to fabricate a veterinary health product.
- The French name of List C was revised to “Liste des produits de santé animale”.
- Proposed subsection C.01.615(1) was revised such that a manufacturer or importer of a VHP will have to notify the Minister at least 30 days before commencing the sale in Canada to allow Health Canada sufficient time to verify that the information in the notification is acceptable.
- VHP manufacturers and importers who have notified under subsections C.01.615(1) and (2) will be required to re-notify of any change to items in paragraphs C.01.615(2)(a) to (h) at least 30 days before the sale of the changed product so that Health Canada will be aware of any changes made to a VHP.
- The annual report required under subsection C.01.612(2) will be required to be submitted by March 31 of the following year to allow more time for the collection of data and preparation of the report.
- Section C.01.600 and paragraph C.01.604(b) of the FDR were amended to indicate that these requirements to label a veterinary drug with “For Veterinary Use Only” or “Veterinary Use Only” do not apply to a VHP. As VHPs will be required to have “Veterinary Health Product” on the label, the additional statements were considered to be unnecessary.
- The coming into force of the amendment to Division regulations respecting GMP and EL requirements for active pharmaceutical ingredients has been extended to 12 months following publication in the *Canada Gazette*, Part II. The coming into force of other aspects of the regulations remains at 6 months.
- Persons who conduct regulated activities may continue to do so without an EL provided they have filed an application for an EL within 14 months following the coming into force of the new regulations respecting GMP and EL requirements for active pharmaceutical ingredients to allow more time for Health Canada to manage the expected number of new EL applications and for affected stakeholders to come into compliance.
- Table II following subsection C.01A.008(4) was revised to include drugs that are on List A as a new category of drugs so as to better track which EL applications are being made in respect of a drug on List A.
- The term “produits de santé vétérinaires” was replaced with “produits de santé animale” to correct the French terminology.

- Websites are now identified as “Government of Canada” rather than “Department of Health,” as per current Government policy.
- Paragraph C.01A.001(2)(d) was revised to clarify that Divisions 1A and 2 do not apply to any veterinary active pharmaceutical ingredients that are not required to be sold by prescription and are a natural health product as defined under the *Natural Health Product Regulations.*
- The amendments to the *Establishment Licensing Fees (Veterinary Drug Regulations)* will come into force 12 months following publication in the *Canada Gazette*, Part II, to accord with the extended coming into force of the EL provisions in the FDR.

Regulatory cooperation

These regulations will bring Canada in closer alignment with international regulatory partners (specifically the United States and the European Union) who already do not allow the importation of unapproved drugs for use in food animals, restrict the use of antimicrobials in the form of APIs, and require that veterinary APIs be compliant with GMPs.

Rationale

The amendments to the FDR are necessary to respond to the serious and growing public health threat of AMR, by improving the regulatory oversight of antimicrobials for veterinary use. In the absence of these regulatory amendments, veterinary antimicrobial APIs not compliant with GMPs that are contaminated with harmful impurities or are sub-potent could be imported or sold in Canada; the own use importation of certain unauthorized drugs for veterinary use, including antimicrobials, would have continued; manufacturers would not have been required to submit important sales volume information by species for veterinary antimicrobials, thereby reducing the efficiency of surveillance programs around antimicrobials; and the availability of VHPs, which could be used as additional tools for managing the health of animals and potentially reducing the need for using antimicrobials, would have continued to be low.

The regulations will be supported by non-regulatory instruments, such as guidance documents, best practices and collaborative approaches with other stakeholders that have a role to play in AMR in Canada.

Implementation, enforcement and service standards

Once the regulations are in force, persons who fabricate, package, label, import or test any API for veterinary use, or perform tests required under Division 2 (GMP), would have to do so in accordance with an establishment licence. In addition, no person will be able to import or sell a veterinary API that was not manufactured according to GMPs as currently set out in Part C, Division 2, of the FDR.

The regulations respecting GMP and EL requirements for veterinary APIs will come into force 12 months after the day on which they are published in the *Canada Gazette*, Part II. All other aspects of the regulations will come into force 6 months following publication in the *Canada Gazette*, Part II. In

addition, persons who fabricate, package, label, test and import veterinary APIs will be permitted to continue conducting those activities without an establishment licence, provided that they have applied for one within 14 months after the coming into force of the applicable regulations. This transition provision will help to ensure that regulated parties do not find themselves in a state of non-compliance once the regulations come into force. Combined, these measures allow for regulated parties to make necessary adjustments to business practices to come into compliance with GMP requirements. Under the *Food and Drugs Act*, regulated parties have the primary responsibility to produce safe products and are expected to take full responsibility for understanding all applicable legislative and regulatory requirements and complying with them.

Policy and guidance documents will outline the type of information that should be submitted in order for Health Canada to verify compliance with the regulations. Compliance and enforcement of the regulations will be done in accordance with a risk-based approach, aligned with departmental policies, including compliance promotion activities.

No service standards will be applicable to the EL application process for veterinary APIs, as no user fee will be charged, but Health Canada expects that the associated process timeline would be comparable to the process timeline for human APIs.

Performance measurement and evaluation

Health Canada will evaluate the implementation of these new regulations in accordance with Treasury Board's Policy on Results. Specifically, key indicators will be monitored and assessed to determine to what extent intended objectives of this proposal are being met.

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Small Business Lens Checklist

1. Name of the sponsoring regulatory organization:

Department of Health

2. Title of the regulatory proposal:

Regulations Amending the Food and Drug Regulations (Veterinary Drugs — Antimicrobial Resistance)

3. Is the checklist submitted with a RIAS for the *Canada Gazette*, Part I or Part II?

☐ *Canada Gazette*, Part I ☑ *Canada Gazette*, Part II

A. Small business regulatory design

I	**Communication and transparency**	**Yes**	
1.	Are the proposed Regulations or requirements easily understandable in everyday language?	☑	
The regulations use language and terminology similar to what is used in the FDR. The RIAS as well as the regulations are d in plain language. Of note, a similar set of regulations regarding the use of human APIs came into force in June 2013.			
2.	Is there a clear connection between the requirements and the purpose (or intent) of the proposed Regulations?	☑	
The amendments will introduce a series of restrictions on the use of antimicrobials in animals. The link between antimicr and resistance has been well documented. Domestic and international pressures have created situations where some ani human infections are untreatable due to antimicrobial resistance (AMR). Therefore, the amendments are anticipated to contribute to the reduction in the incidence of AMR.			
3.	Will there be an implementation plan that includes communications and compliance promotion activities, that informs small business of a regulatory change and guides them on how to comply with it (e.g. information sessions, sample assessments, toolkits, Web sites)?	☑	
The Department plans to introduce a number of communications and compliance promotion activities, which may includ workshops, meetings and webinars. For example, targeted AMR implementation sessions are being planned in webinar f and existing key stakeholder meetings are being leveraged as well to disseminate information on these activities. Health will update its relevant stakeholder guidance documents and Web material.			
4.	If new forms, reports or processes are introduced, are they consistent in appearance and format with other relevant government forms, reports or processes?	☐	
Health Canada will develop an efficient electronic reporting mechanism in order to satisfy the reporting requirements.			
II	**Simplification and streamlining**	**Yes**	
1.	Will streamlined processes be put in place (e.g. through BizPaL, Canada Border Services Agency single window) to collect information from small businesses where possible?	☑	
An electronic notification system has been proposed in the amendments as a means of reducing the paper and reporting			

on all businesses. The entities that will be required to submit volume and species data to Health Canada relating to antim will also have the opportunity to submit this information electronically.		
2.	Have opportunities to align with other obligations imposed on business by federal, provincial, municipal or international or multinational regulatory bodies been assessed?	☑
Canada is a signatory, along with G7 members, to a declaration to reduce AMR through restrictions on the use of antimic The amendments are a major component of satisfying the declaration. Should Canada not proceed with the policies to ac AMR and to align its requirements with international standards for use of antimicrobials in food animals, there may be po implications on trade.		
3.	Has the impact of the proposed Regulations on international or interprovincial trade been assessed?	☑
Consideration has been given to align the amendments with the requirements of international trading partners, such as t United States, the European Union and Japan, to the greatest extent possible. Major risks to trade, specifically the export and poultry products, have been identified as a potential consequence of not introducing the regulations.		
4.	If the data or information, other than personal information, required to comply with the proposed Regulations is already collected by another department or jurisdiction, will this information be obtained from that department or jurisdiction instead of requesting the same information from small businesses or other stakeholders? (The collection, retention, use, disclosure and disposal of personal information are all subject to the requirements of the *Privacy Act*. Any questions with respect to compliance with the *Privacy Act* should be referred to the department's or agency's ATIP office or legal services unit.)	☐
The notification of sale will be reported directly to Health Canada; this information will not be collected by another depar jurisdiction. Information relating to volume and species data will be submitted to Health Canada directly and not collected by another department or jurisdiction. This information could contribute to efforts at the Public Health Agency of Canada and their C Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) project; no information relating to species volume is collected by the Portfolio at this time.		
5.	Will forms be pre-populated with information or data already available to the department to reduce the time and cost necessary to complete them? (Example: When a business completes an online application for a licence, upon entering an identifier or a name, the system pre-populates the application with the applicant's personal particulars such as contact information, date, etc. when that information is already available to the department.)	☐
There has not been a commitment by Health Canada to introduce pre-populated forms. However, the requirement to no Department of sale and reporting of data relating to species and volume is not anticipated to present a significant burden burden would be further reduced through the allowance to submit electronically. These reporting requirements will utiliz existing templates used in other types of drug reporting requirements in the Department.		

6.	Will electronic reporting and data collection be used, including electronic validation and confirmation of receipt of reports where appropriate?	☑
Reporting and notification activities will be eligible for electronic submission.		
7.	Will reporting, if required by the proposed Regulations, be aligned with generally used business processes or international standards if possible?	☑
Similar reporting requirements have been identified in other international jurisdictions, such as the United States and the European Union. The regulations will work within existing generally used business processes.		
8.	If additional forms are required, can they be streamlined with existing forms that must be completed for other government information requirements?	☐
No additional forms will be required.		
III	**Implementation, compliance and service standards**	**Yes**
1.	Has consideration been given to small businesses in remote areas, with special consideration to those that do not have access to high-speed (broadband) Internet?	☑
Consideration has been given to small businesses in remote areas and it has been determined that these businesses will n affected by the amendments.		
2.	If regulatory authorizations (e.g. licences, permits or certifications) are introduced, will service standards addressing timeliness of decision making be developed that are inclusive of complaints about poor service?	☐
No new regulatory authorizations are being introduced with the amendments; the existing performance standard for an establishment licence will continue to be applied.		
3.	Is there a clearly identified contact point or help desk for small businesses and other stakeholders?	☑
The CFIA and RORB will continue to enforce the labelling requirements and to be the contact point for small businesses a stakeholders.		

B. Regulatory flexibility analysis and reverse onus

IV	**Regulatory flexibility analysis**	**Yes**

1.	Does the RIAS identify at least one flexible option that has lower compliance or administrative costs for small businesses in the small business lens section? Examples of flexible options to minimize costs are as follows: • Longer time periods to comply with the requirements, longer transition periods or temporary exemptions; • Performance-based standards; • Partial or complete exemptions from compliance, especially for firms that have good track records (legal advice should be sought when considering such an option); • Reduced compliance costs; • Reduced fees or other charges or penalties; • Use of market incentives; • A range of options to comply with requirements, including lower-cost options; • Simplified and less frequent reporting obligations and inspections; and • Licences granted on a permanent basis or renewed less frequently.	☑

- Veterinary health products will benefit from a less restrictive regulatory framework, where a list of low-risk natur products that meet a list of pre-approved claims will be eligible for sale in Canada once the Department is notifie will avoid the need to file a New Drug Submission in order to sell in Canada.
- Food animal producers will still be eligible to import for own use, provided that the drug does not pose undue sa concerns.

2.	Does the RIAS include, as part of the Regulatory Flexibility Analysis Statement, quantified and monetized compliance and administrative costs for small businesses associated with the initial option assessed, as well as the flexible, lower-cost option?	☑

The RIAS includes a breakdown of compliance and administrative costs. An initial and a flexible option are presented with to GMP and EL activities. Due to improved oversight, the initial option was selected instead of the flexible option.

3.	Does the RIAS include, as part of the Regulatory Flexibility Analysis Statement, a consideration of the risks associated with the flexible option? (Minimizing administrative or compliance costs for small business cannot be at the expense of greater health, security or safety or create environmental risks for Canadians.)	☑

The most commonly identified risk raised with the flexible option is a decrease in inspection oversight; this option was no selected.

4.	Does the RIAS include a summary of feedback provided by small business during consultations?	☐
No individual small businesses were identified during the consultation period and were assumed to be captured through stakeholder organizations during the consultations.		
V	**Reverse onus**	**Yes**
1.	If the recommended option is not the lower-cost option for small business in terms of administrative or compliance costs, is a reasonable justification provided in the RIAS?	☑
Yes, the initial option, although slightly more costly, would increase inspection oversight to ensure animal APIs meet GMI and manufacturing controls.		

- Footnote a
  S.C. 2016, c. 9, s. 8
- Footnote b
  R.S., c. F-27
- Footnote 1
  C.R.C., c. 870
- Footnote 2
  Government of Canada. 2011. *Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) 2008*. Guelph: Public Health Agency of Canada.
- Footnote 3
  Van Boeckel, Thomas P., et al. *Global Trends in Antimicrobial Use in Food Animals*. Proceedings of the National Academy of Sciences (http://www.pnas.org/content/112/18/5649.full).
- Footnote 4
  Canadian Antimicrobial Resistance Surveillance System—Report 2015. Available at http://healthycanadians.gc.ca/publications/drugs-products-medicaments-produits/antibiotic-resistance-antibiotique/antimicrobial-surveillance-antimicrobioresistance-eng.php.
- Footnote 5
  The Chief Public Health Officer's Report on the State of Public Health in Canada, 2013: Infectious Disease—The Never-ending Threat (http://www.phac-aspc.gc.ca/cphorsphc-respcacsp/2013/index-eng.php).
- Footnote 6
  WHO Global Principles for the Containment of Antimicrobial Resistance in Animals Intended for Food. June 2000.

- Footnote 7
  European Center for Disease Prevention and Control and European Medicines Agency joint technical report. *The bacterial challenge: time to react*. 2009.

- Footnote 8
  Antimicrobials in Agriculture and the Environment: Reducing Unnecessary Use and Waste, The Review on Antimicrobial Resistance. 2015.

- Footnote 9
  Public Health Agency of Canada. 2013. Canadian Integrated Program for Antimicrobial Resistance Surveillance [Custom Data File].

- Footnote 10
  Government of Canada. 2012. *Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) 2011 —Antimicrobial Resistance Short Report*. Guelph: Public Health Agency of Canada.

- Footnote 11
  Public Health Agency of Canada. 2007. Salmonella *Heidelberg Ceftiofur-Related Resistance in Human and Retail Chicken Isolates*.

- Footnote 12
  WHO Global Principles for the Containment of Antimicrobial Resistance in Animals Intended for Food. June 2000.

- Footnote 13
  2015 Spring Reports of the Auditor General of Canada. *Report 1—Antimicrobial Resistance*. Available at http://www.oag-bvg.gc.ca/internet/English/parl_oag_201504_01_e_40347.html.

- Footnote 14
  Natural health products for human use are regulated under the *Natural Health Products Regulations* (NHPR) while these same drugs when used in animals are regulated under the *Food and Drug Regulations*. An authorization issued under the NHPR does not apply for the sale of the same drug in animals.

- Footnote 15
  Information about the Interim Notification Pilot Program (INPP) is available at http://www.hc-sc.gc.ca/dhp-mps/vet/issues-enjeux/notification-declaration-eng.php.

- Footnote 16
  The list of substances of the INPP formed the basis for List C of the proposed regulations. This list is available at https://www.lrvhp.ca/substances/.

- Footnote 17
  Information about the EDR program is available at http://www.hc-sc.gc.ca/dhp-mps/vet/edr-dmu/index-eng.php.

- Footnote 18
  A copy of List A is available by request from the contact identified at the end of the Regulatory Impact Analysis Statement (RIAS).

- Footnote 19
  A copy of List B is available by request from the contact identified at the end of the RIAS.

- Footnote 20
  A copy of List C is available by request from the contact identified at the end of the RIAS.

- Footnote 21
  Bengtsson, B. and Wierup, M. 2006. "Antimicrobial Resistance in Scandinavia after a Ban of Antimicrobial Growth Promoters." *Animal Biotechnology*, 17:2.

- Footnote 22
  CDC, *Antibiotic Resistance Threats in the United States, 2013* is available at http://www.cdc.gov/drugresistance/threat-report-2013/.

- Footnote 23
  Assumes that EL fees would be charged due to amendments to the *Fees in Respect of Drugs and Medical Devices Regulations*.

- Footnote 24
  Health Canada's Task Force on Own-Use Importation (OUI) Final Report — August 5, 2008, available at https://www.canadianveterinarians.net/documents/task-force-reporton-own-use-importation.

- Footnote 25
  Technical discussions on veterinary drugs regulatory modernization, available at http://www.hc-sc.gc.ca/dhp-mps/ consultation/vet/discussions-eng.php.