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IMPROVING ACCESS TO VETERINARY PHARMACEUTICALS, VETERINARY HEALTH PRODUCTS, LIVESTOCK FEEDS AND VETERINARY BIOLOGICS IN CANADA

[THIS DOCUMENT IS ENDORSED BY MAJOR ORGANIZATIONS REPRESENTING CANADA'S FARMED ANIMAL PRODUCERS;VETERINARIANS, VETERINARY PHARMACEUTICAL AND ALTERNATIVE PRODUCT MANUFACTURERS;AND FEED PROVIDERS]

Contents

List of Organizations Endorsing this Document (Alphabetical)

Animal Nutrition Association of Canada

Canadian Animal Health Institute

Canadian Association of Bovine Veterinarians

Canadian Association of Swine Veterinarians

Canadian Aquaculture Industry Alliance

Canadian Cattle Association

Canadian Equine Veterinary Advocacy Alliance

Canadian Federation of Agriculture

Canadian Hatching Egg Producers

Canadian Pork Council

Canadian Sheep Federation

Canadian Veterinary Medical Association

Chicken Farmers of Canada

Dairy Farmers of Canada

Egg Farmers of Canada

Turkey Farmers of Canada

Glossary of Terms

Veterinary Health Products: Veterinary Health Products are considered low risk drugs in dosage form with an intended use to maintain and promote health and wellbeing in animals, including food and companion animals. (web reference: https://health-products.canada.ca/vhp-psa/en/about/1)

Veterinary Biologics (including vaccines): Veterinary biologics are animal health products such as: vaccines, antibody products, and in vitro diagnostic test kits that are used for the prevention, treatment, or diagnosis of infectious diseases in animals, including domestic livestock, poultry, pets, wildlife, and fish. Veterinary biologics are regulated by the Canadian Food Inspection Agency (CFIA). (web reference: https://inspection.canada.ca/animal-health/veterinary-biologics/eng/1299159403979/1320545281259)

Livestock Feeds: The manufacture, sale and import of livestock feeds are regulated in Canada under the *Feeds Act* and regulations and *Health of Animals Act* and regulations, administered by the CFIA. (web reference: https://inspection.canada.ca/animal-health/livestock-feeds/eng/1299157225486/1320536661238)

Veterinary Drugs/Pharmaceuticals: https://www.canada.ca/en/health-canada/corporate/mandate/regulatory-role/what-health-canada-regulates-1/veterinary-drugs.html

Regulatory Fees (effective April 1, 2024): https://www.canada.ca/en/health-canada/services/drugs-health-products/funding-fees/veterinary-drugs/submission-evaluation-fees.html

One Health: One Health is an integrated approach to the fight against infectious diseases. The One Health approach stresses the interconnections between human, animal and environmental health.

Farmed animals: This term is used throughout the document as a collective term to refer to cattle, horses, sheep, goats, swine, chickens, turkeys, ducks, geese, fish and other species reared in commercial aquaculture production.

Pan-Canadian Action Plan on Antimicrobial Resistance: https://www.canada.ca/en/public-health/services/publications/drugs-health-products/pan-canadian-action-plan-antimicrobial-resistance.html

Executive Summary

Canadian farmers and veterinarians recognize the inter-relatedness of human, veterinary, and environmental health expressed in the concept of 'One Health' and understand the role they play in the success of the Pan-Canadian Action Plan on Antimicrobial Resistance. To best play their part in a One Health approach, farmers and veterinarians urgently need increased access to a wide range of tools that will prevent and control illness and promote the health and wellbeing of animals. Simply stated: the more varied tools available to farmers and veterinarians, the less they must rely on products to maintain animal health and wellbeing that are highly important to human health.

The tools currently available fall into several different categories, based on how they are used. These include: veterinary pharmaceuticals; veterinary health products; feed and water additives; vaccines; parasiticides and pesticides that help maintain animal health; and livestock feeds which help ensure nutritional requirements and meet and support optimal functions in animals related to their physiological states. Each of these categories has different regulatory oversight and approval processes.

Due to various barriers detailed in this Whitepaper, Canadian farmers' and veterinarians' access to such tools is virtually at a crisis point, which is compounded by the fact that the number of currently approved and available tools is eroding at a significant rate. The result is that Canadian farmers and veterinarians are forced to rely on an increasingly limited number of tools – many of which are also important in human medicine. Not only does this have implications for animal and human health, it places Canada at a competitive disadvantage compared to other countries who do have access to such tools.

Over the past year, organizations from across the agricultural sector have come together to identify barriers preventing the access of these critical tools, and to jointly propose a series of consensus solutions. Participants in this initiative include major organizations representing Canada's farmed animal producers; veterinarians, veterinary pharmaceutical and alternative product manufacturers; and feed providers.

Summary of Solutions Detailed in this Whitepaper

If enacted, any of the solutions outlined below will help improve access to critical veterinary tools, which, in turn, will better position Canadian farmers and veterinarians to play their part in a One Health approach.

*Note that the solutions below are numbered in order of appearance in the document, not in terms of their relative priority.

1) **As Health Canada is assessing the feasibility of a Pull Incentive model for human antimicrobials, it should consider the feasibility of a similar model for veterinary antimicrobials which provides guaranteed ROI for companies who successfully bring their products to market in Canada. Any model should also incentivize the retention of existing antimicrobials or return of previously marketed antimicrobials that are of lesser importance to human medicine.**

2) **Reduce approval costs and prioritize animal health and food security by allowing the approval in Canada of veterinary pharmaceuticals already approved by trusted regulatory authorities licenced in other jurisdictions (US, UK, EU, Australia, New Zealand).**

3) **Immediately halt all planned fee increases related to the approvals, review and maintenance of veterinary pharmaceuticals, veterinary biologics, veterinary health products and pesticides and alternatives (SOR/2019-124); consider rolling back fees to 2020 levels.**

4) **Provide increased flexibility in any uniquely Canadian requirements governing Good Manufacturing Practices for Active Pharmaceutical Ingredients, specifically in terms of extending the list of approved foreign inspection agencies or corporate/consult audit reports.**

5) **Examine opportunities to harmonize requirements and inspections of manufacturing facilities for veterinary pharmaceuticals with trusted jurisdictions to reduce costs while maintaining food safety.**

6) **Create a set of eligibility criteria for rolling reviews specifically for veterinary pharmaceuticals, including both those seeking approval that had previously been available and those seeking re-approval, as part of standard process. Permit a pre-determined 'grace period' for products that have gone dormant or been cancelled post-market wherein a company could seek re-approval without restarting the approvals process.**

7) **Improve and increase regulatory flexibility for low-risk Veterinary Health Products (VHPs) and feed additives by:**
    a. **Increasing the range of efficacy and prevention claims permitted on the label of feed and water additives and VHP's intended for use in food-producing animals (e.g. positive effects on pathogens and diseases);**
    b. **Permitting the use of individual VHPs in combination with other VHPs;**
    c. **Establishing a system to allow feed and water additives and VHPs approved in trusted jurisdictions to be allowed for use in Canada (e.g. Bill C-359);**
    d. **Institute changes to improve regulatory performance to more closely match stated performance targets.**

8) **Create a process where inactivated vaccines that are conditionally approved in the US can be evaluated and similarly approved in Canada.**

9) **Re-evaluate restrictions on the use of autogenous vaccines, with a view to increasing the flexibility of their use within an animal production system while still mitigating any risks.**

Introduction

Farmed animal production and welfare requires that veterinary health professionals have access to tools that will prevent and control illness and promote the health and wellbeing of animals. For most farmed animals, the major health risks are infectious diseases. As a result, the tools most needed are those used to promote health and to control, prevent and treat common infectious diseases. Unfortunately, due to a number of barriers, Canadian livestock farmers' access to such tools is virtually at a crisis point. Not only does this have implications for animal and human health, it also places Canadian farmers at a competitive disadvantage compared to farmers in other countries who do have access to such tools.

Our organizations, representing Canada's farmers, veterinarians, veterinary pharmaceutical and alternative product manufacturers, and feed providers, have come together to propose solutions which will help to address some of the barriers preventing access to these critical products. If implemented, the solutions described in this document will help provide farmers access to the tools they need to best play their part in a 'One Health' approach. We ask the government to take urgent action to address these complex issues.

Categories of Tools Currently Available

The tools currently available to prevent, control and treat illness, and to promote animal health and wellbeing fall into several categories, based on how they are used:

- Pharmaceuticals, which are used for treatment to restore or maintain health;
- Veterinary Health Products (VHPs), formerly known as low-risk animal health products that have become available within the past decade;
- Parasiticides and pesticides, which are used to treat and control internal and external parasites in order to maintain animal health;
- Vaccines to prevent disease (a cornerstone of infectious disease preventive strategies);
- Feed and water additives that help maintain animal health; and,
- Livestock feeds which help ensure nutritional requirements and meet and support optimal functions in animals related to their physiological states.

Each of these categories of tools has different regulatory oversight and approval processes.

Unique Business Models for Canadian Farmed Animal Sectors

The business models for each farmed animal industry in Canada are unique. Some Canadian food animal commodities, such as the swine and beef sectors, supply the domestic market but also export a substantial component of their overall production. This means that Canadian swine and beef producers compete directly with swine and beef producers in other exporting countries, as well as with swine and beef producers in countries that import Canadian meats. Other Canadian food animal commodities, such as dairy, poultry and sheep, are more focused on the domestic market – but they are competing directly with producers in countries that export dairy, poultry and sheep products to Canada as permitted by negotiated trade agreements. Whether in relation to international or domestic markets – those international competitors often have access to a wider range of animal health products (e.g. pharmaceuticals, feed and water additives, parasiticides, vaccines) which are not available to producers in Canada. Since optimal animal health is a significant contributor to production efficiency, lack of

access to these critical products can place Canadian producers at a competitive disadvantage relative to producers in other food and livestock producing nations.

In addition, farmed animal production occurs within a social context. This is reflected through the current emphasis on an integrated 'One Health' approach to animal management. A robust commitment to the One Health approach requires Canadian farmed animal producers to have access to tools that allow them to make animal management decisions that can consider the integrated health environment that this approach is designed to foster. Successfully implementing a One Health approach requires farmed animal industries to have access to a range of treatment options (e.g. access to antimicrobial drugs of lesser importance to human medicine), to effective preventive options (e.g. vaccines against both major and minor pathogens) and to tools to promote and maintain good health (e.g. VHP's, livestock feeds such as gastrointestinal modifiers).

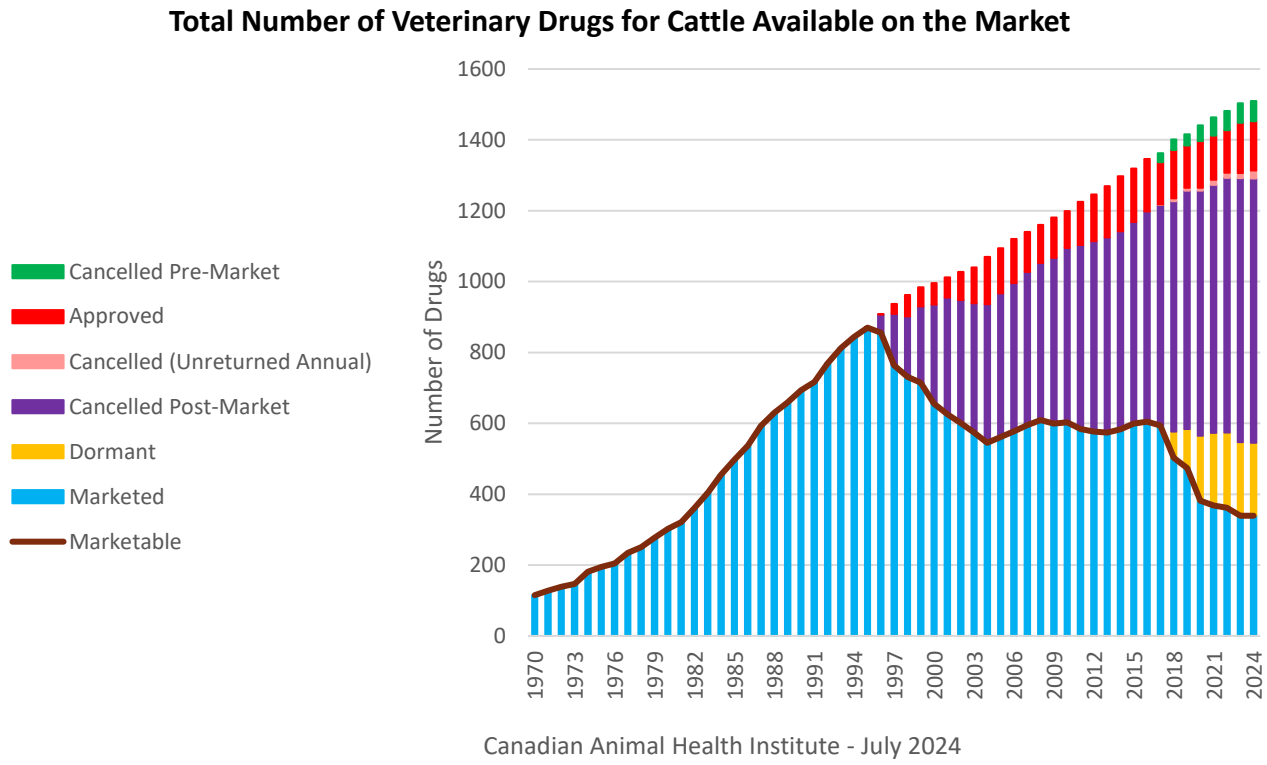
Successful management of antimicrobial use (AMU) and antimicrobial resistance (AMR) must also be achieved through a One Health approach. It is equally probable that failure to consider a One Health approach is likely to make antimicrobial stewardship goals more difficult to attain.

The Current Situation with Availability of Veterinary Pharmaceuticals in Canada

In the past several decades, there has been an erosion in the tools available for use in farmed animal production. One of the most obvious examples of these losses is the decline in the number of pharmaceuticals that are available for use in Canada. Figure 1 (below) presents data of pharmaceuticals available for treatment of cattle. Much of these data are historical, but considering only the last five to six years, the number of pharmaceuticals that are approved but unavailable has reached the point where the number of products that are actually available makes up less than 50% of the number of products that are approved for use in cattle in Canada.

According to data derived from Health Canada's online Drug Product Database, between 2017 and 2022, the number of licensed veterinary medicines (i.e. products that have been assigned a Drug Identification Number or DIN) that were actually sold in Canada decreased by 40%. The reality is that Canadian veterinarians and farmers currently have access to many fewer licensed veterinary drugs than they did as recently as six years ago. The Canadian Animal Health Institute's (CAHI's) Priority Animal Health Needs Report, presented to officials from Health Canada's Veterinary Drug Directorate in January 2023, notes that the rate of loss of veterinary pharmaceuticals, especially pharmaceuticals approved for the treatment of cattle, has accelerated since 2018 (please refer to Figure 1). The situation is similar for other farmed animal species (please refer to Appendix 1).

Figure 1. Total number of veterinary drugs available (for cattle only) annually between 1970 and 2022 based on their status as reported in the Health Canada Drug Product Database.



Except in very few cases, it is not possible to determine why individual products become dormant[1]. It is likely there are several factors, either individually, or in combination, that contribute to the lack of availability of individual products. That does not imply that a single action might not help stop the loss of products; rather it implies that a broad approach to the issue is likely to be more successful than any one individual change.

Although many approved pharmaceutical drugs are no longer available in Canada, the health situations that required their use have not gone away. One direct consequence of this is that veterinarians find it necessary to use pharmacies to compound products that are similar to products that had been available in the past. Such compounded pharmaceuticals have not been subjected to the same quality and safety evaluations that registered pharmaceuticals must undergo. Similarly, the lack of treatment options makes it difficult to treat animals with some common diseases; many pharmaceuticals which have gone dormant were the only approved treatments for some of these common diseases. As a consequence, veterinarians must now write prescriptions to allow the use of the remaining accessible pharmaceuticals so they will be used in an extra-label manner[2]. Extra-label use and the use of compounded medication in food- producing animals creates a situation where individual veterinarians must assume the food safety risks associated with those treatments.

[1] The Health Canada Drug Product Database defines 'dormant' as meaning that there were no records of sales for that product within the previous 12 months, but does not provide rationale for dormancy.
[2] 'Extra-label manner' refers to the use or intended use of a drug approved by Health Canada in an animal or in a manner not in accordance with the label or package insert.

Dealing with the loss of pharmaceuticals is only one of the challenges that Canadian farmed animal producers and veterinary professionals face. The lack of available veterinary pharmaceuticals accentuates the lack of access to other tools that could be used to maintain farmed animal health, welfare and production. These other tools include access to a wider range of vaccines to prevent infectious diseases and greater access to VHP's, feed and water additives, whose main benefits are to support health and wellbeing rather than target individual diseases.

Increasing Social Focus on Antimicrobial Stewardship

As noted above, Canadian farmers and veterinarians recognize the inter-relatedness of human-veterinary-environmental health expressed in the concept of One Health. Canadian farmers and veterinarians also recognize that they play roles in the success of the Pan-Canadian Action Plan on Antimicrobial Resistance (PCAP) especially in regard to Pillars of Action 2 through 5.

Canadian farmers work closely with veterinarians to abide by both Federal and Provincial guidelines that are intended to assure that antimicrobials used on farms are used prudently. Farmers understand that ensuring robust and healthy animals is the best way to minimize the use of antimicrobials. This is one reason why they routinely collaborate with veterinarians to evaluate the health status of their herds and flocks, implement biosecurity measures and review disease prevention protocols to identify opportunities for improvement. Farmers are best able to implement improvements when they have appropriate tools to do so.

Responsible use of antimicrobials, in combination with other animal health tools (e.g. vaccines, VHP's and feed additives) is also essential to reduce suffering and promote welfare, while preserving efficacy. In addition, to help monitor the risk that antimicrobials will become ineffective, and to contain the emergence and spread of resistant bacteria among animals, food, and people, Canadian farmers and veterinarians work in partnership with Health Canada and the Public Health Agency of Canada through the Canadian Integrated Program for Antimicrobial Resistance (CIPARS). CIPARS collects, analyses and communicates trends in antimicrobial use and in antimicrobial resistance for select bacteria from humans, animals and retail meat across Canada. This collaboration ensures robust surveillance and publicly available analysis of data on antimicrobial use and resistance on farms. The methodology and data collection are actively and regularly reviewed to ensure their value to the country and consumers.

Health Canada has created four categories of antimicrobials based on their importance to human medicine. One essential action in antimicrobial stewardship is choosing to use an effective antimicrobial that is of lower importance to human medicine when making therapeutic decisions. When there are few available antimicrobial choices or no alternative treatment options, veterinarians and farmers must make difficult decisions. Within some jurisdictions, regulators are seeking to reduce the use of antimicrobials by reserving certain antimicrobials for human use only (such as those in Health Canada's Category I, which are considered of very high importance).

Canadian farmers and veterinarians recognize that reducing the use of antimicrobials categorized as important to human medicine is a critical aspect of prudent antimicrobial stewardship. However, while the EU and other competing jurisdictions like the United States (US) have many approved alternatives to such antimicrobials, including antimicrobials of lesser importance to human medicine, Canada currently does not. This is particularly true in relation to the management of infectious diseases in lactating dairy cows, where licensed alternatives to "Category 1" antimicrobials are extremely limited. Another

example is *Streptococcus suis,* a common bacterium that can cause multiple health problems in swine, which is challenging to manage due to a lack of approved treatment options that have either short enough withdrawal times or a long enough duration of efficacy.

Identifying Barriers and Proposing Solutions: Accessing Veterinary Pharmaceuticals

There are a number of barriers which can serve to disincentivize companies and prevent the access and approvals of veterinary pharmaceuticals in Canada. To help overcome these barriers, our organizations collectively propose several potential solutions. For clarity, we have grouped these barriers and solutions together into three main themes: limited potential return on investment, high fees to obtain and retain market authorizations, and challenges with the regulatory process in Canada.

Barrier 1: Limited Potential Return on Investment for Veterinary Pharmaceuticals

Almost all pharmaceuticals are developed by multinational companies. These companies are businesses that understandably focus on gaining access to markets for their products, or on developing products for market segments in countries where they are likely to lead to a return on investment (ROI). Unfortunately, the reality is that Canada is a highly regulated country with a small potential market for veterinary pharmaceuticals, veterinary vaccines, and products classified as VHPs which means a low potential ROI for companies investing in this market.

Agricultural commodities, including farmed animals, are particularly sensitive to input costs (eg. feed, fertilizer, fuel, veterinary pharmaceuticals, vaccines, and health products, etc.). When it comes to veterinary pharmaceuticals, vaccines, and other VHPs, the impact of rising input costs can be accentuated because Canadian farmers must compete with countries with lower animal health care costs. This creates a climate where farmers and veterinarians must continually balance costs against benefits; these realities impact how easily animal health companies can pass along their costs to farmers in Canada.

Farmed animal populations define market size and sales potential for veterinary products. Market size is thus a major determinant in the potential for ROI, and therefore, on the relative attractiveness of a market for product manufacturers. The recently released livestock census data for Canada documents that the national cattle herd is at its lowest level in decades[3]. Livestock and poultry populations in other jurisdictions, such as the US and the EU, are considerably larger than those in Canada. Even smaller countries, like Australia and New Zealand, Canada's main competitors in beef, dairy, and lamb exports, have agricultural animal populations much larger than Canada's – making them more attractive as potential marketplaces for veterinary products. In fact, the Canadian market is equivalent to only 10% of US sales in animal health products and represents just 2.5% of global sales.

Compounding the impact of small market size, some veterinary products require a greater level of investment to achieve regulatory approval than others. Antimicrobials are extremely costly and time-consuming to research and develop. Adding to the problem, once they are marketed, their use can lead to a risk that bacteria and other microbes will develop resistance, potentially leading to decreased

[3] https://www150.statcan.gc.ca/n1/daily-quotidien/230228/dq230228e-eng.htm

effectiveness and gradually reducing their value to the healthcare system, as well as their economic value, over time. The end result is a financially unattractive business model for antimicrobials in Canada with low potential for sales and high potential for negative ROI for companies.

'Pull Incentives': A Novel Approach to Veterinary Antimicrobials

In 2022, Health Canada published a Best Brains Exchange Summary Report entitled: *Challenges in the Antimicrobial Business Model and Potential Incentives to Increase Access and Promote Innovation*[4]. The report recognizes that 'market failure' – when the cost of developing a new health product and/or maintaining it on the market exceeds the revenues generated from its sale – impacts antimicrobials and serves as a significant barrier to their development. In response to this challenge, participants in the Best Brains Exchange generally agreed that Canada should explore a 'Pull Incentive' model to support antimicrobial innovation and improve access in relation to human drugs. This is a model that our organizations would also support exploring as a potential mechanism to help ensure a more stable and predictable ROI for companies who produce critical veterinary products that are considering entering the Canadian market.

Given that the use of antimicrobials limits their utility over time, and that reducing AMR is both a societal and governmental priority, a market model for antimicrobials that is solely based on volume sold is not aligned with public health objectives. In recognition of the overarching societal benefits of defending antimicrobial efficacy, 'Pull Incentives' are a mechanism that would reward companies for the successful innovation, development, and commercialization of critical veterinary products. The advantage of such a model is that it provides guaranteed ROI for companies who successfully bring their products to market in Canada, assuring greater product availability, while also aligning with public health objectives.

While Pull Incentive models for human medicine tend to focus on incentivizing the development of novel products, in veterinary medicine, the focus should likely include incentivizing the retention of existing antimicrobials or return of previously marketed antimicrobials that are of lesser importance to human medicine. Veterinary products of lesser importance to human medicine are often generic pharmaceuticals, with limited potential for profitability, and would therefore benefit significantly from a Pull Incentive model.

Many countries, including the UK, US, and EU are already piloting or developing Pull Incentive models for human antimicrobials within their own jurisdictions. These include several different types of Pull Incentives, such as: extensions of patent protections, tradeable vouchers that extend the exclusivity of a qualifying drug, high per-unit prices, annual revenue guarantees, and subscriptions.

In a recent report on Pull Incentives for human drugs in a Canadian context requested by the Public Health Agency of Canada (PHAC)[5], the Canadian Council of Academies expert panel concluded that a Subscription Pull Incentive (SPI) model would work best for a country like Canada. SPI models provide companies with a negotiated fixed annual payment, based on a limited window of eligibility (e.g.: 3-to-5

[4] Health Canada. (2022). *Best Brains Summary Report: Challenges in the Antimicrobial Business Model and Potential Incentives to Increase Access and Promote Innovation.* https://www.canada.ca/en/health-canada/services/publications/drugs-health-products/best-brains-exchange-meeting-antimicrobial-resistance.html

[5] Canadian Council of Academies. (2023). *Overcoming Resistance: Expert Panel on Antimicrobial Availability.* https://cca-reports.ca/reports/pull-incentives-for-high-value-antimicrobials, 2023.

year contracts, with an option to extend to 10 years). This guarantees companies a pre-determined income, regardless of sales. In the report, the expert panel notes that the strengths of SPI models include their ability to adjust incentives over time as new evidence emerges, an incentive structure that supports equitable access but does not encourage overuse, and an ability to create contractual obligations that improve drug availability. In order to best equip farmers to play their expected roles when it comes to protecting health and welfare while practicing antimicrobial stewardship in Canada, additional antimicrobial products are urgently needed on the Canadian market.

Even though such discussions have thus far been primarily focused on strategies for human antimicrobials, our organizations welcome similar discussions with both Health Canada and PHAC relating to Pull Incentives or other potential incentives for veterinary antimicrobials that are of lower importance to human medicine. Given the many disincentives that exist for veterinary pharmaceutical companies seeking to enter the Canadian market, and the critical importance of reducing overreliance on currently available antimicrobials, it is time for the government to look outside of the traditional pay-per-unit model and consider alternative approaches.

Proposed Solution: Limited Potential Return on Investment

In order to address this barrier, our organizations strongly recommend implementing the following solution as soon as possible:

1) **As Health Canada is assessing the feasibility of a Pull Incentive model for human antimicrobials, it should consider the feasibility of a similar model for veterinary antimicrobials which provides guaranteed ROI for companies who successfully bring their products to market in Canada. Any model should also incentivize the retention of existing antimicrobials or return of previously marketed antimicrobials that are of lesser importance to human medicine.**

Barrier 2: High Fees for Regulatory Oversight of Veterinary Pharmaceuticals

In addition to the limited potential for ROI in the Canadian market, Canadian fees for application and approvals of veterinary pharmaceuticals are far out of step with the relative size of the marketplace. According to data presented on cost recovery by Health Canada at a meeting of industry and government stakeholders on January 23, 2023, regulatory fees in Canada are generally much higher than fees in Australia, and are comparable to bigger animal health markets, such as the US. Fees for review of new veterinary drug submissions in Canada may even exceed those in much larger markets, such as the EU. Further compounding this issue is that the Canadian fee structure does not consider the size of the sectors that are the intended users of the product. That means that although regulatory fees may impact the entire Canadian livestock community, the impact is even more significant when the size of the commodity is small.

Furthermore, there is a significant disparity between Canadian fees associated with obtaining a veterinary drug establishment license and fees to obtain the same license in other jurisdictions, such as Australia, and the UK. Drug establishment licences must be obtained for any facility that manufactures human and veterinary drugs that will be sold in Canada. There are two types of facilities involved in the manufacture of veterinary drugs: those that manufacture the active pharmaceutical ingredient (API), and those that manufacture the finished product. In a Canadian context, the costs of maintaining

licenses for each of these facilities are borne by pharmaceutical companies, when often, the same facilities have already been inspected and licensed by other jurisdictions. This may provide opportunities for additional collaboration between Canada and other jurisdictions. Canada has mutual recognition agreements in place with most EU states, indicating that the inspections and licensing of the facilities in these geographies are equivalent to Canada's. It is recommended that mutual recognition be extended to include the US, Australia, and New Zealand.

While current Canadian fees for regulatory reviews and ongoing oversight of licensed veterinary pharmaceuticals are already out of line with the size of our domestic market, in 2020, the government initiated a plan to increase these fees by 500% by 2027 (SOR/2010-124). These planned cost recovery increases come on top of additional anticipated yearly increases which are indexed to the Consumer Price Index (CPI). Unlike markets where product registration and regulatory service fees can be spread across larger animal populations with associated larger potential sales, in Canada, these costs are concentrated in smaller populations so that all costs are spread over a much smaller volume of veterinary drugs sold.

Proposed Solutions: High Fees for Applications and Approvals

In order to address these barriers, our organizations strongly recommend implementing the following solutions as soon as possible:

1) **Reduce approval costs and prioritize animal health and food security by allowing the approval in Canada of veterinary pharmaceuticals already approved by trusted regulatory authorities licenced in other jurisdictions (e.g. US, UK, EU, Australia, New Zealand).**

2) **Immediately halt all planned fee increases related to the approvals, review and maintenance of veterinary pharmaceuticals, veterinary biologics, veterinary health products and pesticides and alternatives (SOR/2019-124); consider rolling back fees to 2020 levels.**

Barrier 3: Regulatory Barriers for Veterinary Pharmaceuticals

There are several additional barriers related to the broader regulatory environment that serve to prevent access to veterinary pharmaceuticals; these are summarized below:

<u>GMPs for APIs</u>

In 2017, Health Canada introduced regulatory changes which increased Good Manufacturing Practice (GMP) requirements for Active Pharmaceutical Ingredients (APIs) to require Drug Establishment License (DEL) listings. While such changes were made to improve oversight, they inadvertently put the availability of veterinary pharmaceuticals in Canada further at risk. Given that many foreign API providers service multiple countries, this represents an additional cost to meet Canadian regulatory requirements. The end result is a significant increase in the costs of Canadian drug components manufactured at such sites, while also potentially contributing to disruptions in the availability of those products.

In addition to increased costs, some API sites are not able to meet the new Canadian requirements. This is particularly important for those who manufacture low-risk APIs, which are treated as food ingredients in other markets (which comes with a lower burden of evidence). In other cases, API sites may be

discouraged from meeting Canadian requirements when GMP evidence is considered sufficient for a product by regulators in other larger markets, but which is not recognized as sufficient for the same product to be sold in Canada. Canada's robust requirements for on-site inspection of foreign sites have proven to be an additional hurdle, given these requirements go above and beyond what is required for compliance in larger markets like the EU and the US.

These new requirements have already caused at least one commonly used bovine mastitis treatment to be removed from the Canadian market because the manufacturer was unable to find an API site compliant with the new Canadian GMP requirements. While appropriate oversight over the manufacture of pharmaceuticals and ingredients remains paramount, it will be important to provide significantly increased flexibility in any uniquely Canadian requirements, specifically in terms of extending the list of approved foreign inspection agencies or corporate/consult audit reports.

A Call for Implementation of Rolling Reviews

In its recent consultation on proposed agile regulations and guidance for licensing drugs and medical devices, Health Canada proposed guidelines which will make it possible to submit veterinary drugs through a Rolling Review Application Package (RRAP) on an emergency basis. However, the eligibility criteria described within the guidelines are limited to novel products and tailored for human products and human health conditions. Veterinary products may not easily fit these criteria, and the proposed regulations explicitly exclude generic products. As previously noted, facilitating the approval of generic products will play an important role in veterinary medicine when it comes to supporting antimicrobial stewardship.

Our organizations strongly support any initiative designed to facilitate submission of requests for approval of new veterinary pharmaceuticals on the Canadian market. We therefore consider it important to make available a set of eligibility criteria for rolling reviews created specifically for veterinary pharmaceuticals, and that rolling reviews for veterinary pharmaceuticals be implemented as part of standard process (not solely in case of emergencies). Furthermore, given the high volume of products that have gone dormant from the Canadian market or been cancelled post-market due to many of the barriers outlined in this document, veterinary pharmaceuticals seeking approval that had previously been available should also be eligible for a rolling review process. As an additional measure, any product that has gone dormant from the Canadian market or been cancelled post-market should be given a 'grace period' wherein a company could seek re-approval for that product without being required to restart the approvals process from the beginning as if it were a new drug.

Proposed Solutions: Regulatory Barriers for Veterinary Pharmaceuticals

In order to address these barriers, our organizations strongly recommend implementing the following solutions as soon as possible:

1) **Provide increased flexibility in any uniquely Canadian requirements governing GMPs for APIs, specifically in terms of extending the list of approved foreign inspection agencies or corporate/consult audit reports.**

2) **Examine opportunities to harmonize requirements and inspections of manufacturing facilities with trusted jurisdictions to reduce costs while maintaining food safety.**

3) **Create a set of eligibility criteria for rolling reviews specifically for veterinary pharmaceuticals, including both those seeking approval that had previously been available and those seeking re-approval, as part of standard process. Permit a pre-determined 'grace period' for products that have gone dormant or been cancelled post-market wherein a company could seek re-approval without restarting the approvals process.**

Identifying Barriers and Proposing Solutions: Veterinary Health Products (VHP's) and Feed Additives

While veterinary pharmaceuticals are generally regarded as the major tool in managing health and disease, when treatment options become as limited as they are today, the need for alternative health solutions becomes even more urgent. For example, feed and water additives and VHP's can also play a critical role in supporting good animal health and in turn, reduce disease.

The Need to Expand the VHP Program

The VHP program is a positive development; however, modifications to the VHP program would help it better meet the needs of Canadian agriculture.

One notable limitation is that individual VHPs cannot be used in combination with other VHP's. Permitting such combinations will allow for the expansion of antibiotic reduction programs and will be consistent with the field programs that currently employ multiple feed additives.

As the VHP program matures, there needs to be a continued focus to ensure operational effectiveness for use in livestock and poultry production.

Scope of Claims Allowed for VHP's and Feed Additives

The range of claims currently allowed for VHPs and feed additives should be expanded to recognize the changing landscape in research related to their role in animal health - provided those efficacy claims are supported by appropriate research findings. As an example, research in Canada and around the world has already assessed the efficacy and safety of various feed additives with the goal of supporting animal health and reducing the incidence or impact of disease. Improvements in overall health will, in turn, reduce the need to resort to treating with antimicrobials and these tools can have a beneficial impact on pathogens. Currently, due to regulatory constraints, it is not possible to make these types of claims.

More Efficient Registration of Feed Additives

Water and feed additives have the potential to support and improve animal health and reduce the need for antimicrobial use. However, the regulatory process to have feed additives registered in Canada is lengthy, unpredictable and does not support evolving research and innovation in areas such as pathogen reduction. The CFIA requirements to demonstrate efficacy to substantiate claims, especially in multiple species, are often more burdensome than other jurisdictions and companies are forced to run trials specifically for Canada, which serves as a further disincentive. Similar to veterinary pharmaceuticals, Canada is often one of the last countries considered by multinational companies to bring a feed additive

to market due to the cumbersome and costly regulatory requirements in relation to the size of the market and potential ROI.

The Canadian requirements for feed additive registration compared to our largest trading partner, the US, often means producers in the US have access to feed additives that Canadian producers do not. For many types of feed additives where companies wish to market their product without any claims, the US only requires companies to demonstrate safety of products; on the other hand, Canada does not allow feed additives to be marketed without claims, thereby requiring both safety and efficacy to be demonstrated. This provides a competitive advantage to international producers as they have access to a larger suite of feed additives than Canadian producers.

The significant amount of time it takes for a new feed additive to be registered in Canada is also a disincentive for companies. Currently, it takes two to three years to have a new feed additive registered, where CFIA's service standard is 90 days. By the time companies decide to file an application in Canada and get their product registered, it has often been on the market in other jurisdictions for quite some time and is no longer a new innovative product. The Animal Feed Division urgently needs more resources to be able to register new feed additives in a timely manner and give Canadian producers access to these new tools at the same time as their counterparts in other countries.

Proposed Solutions: VHP's and Feed Additives

In order to address these barriers, our organizations strongly recommend implementing the following solutions as soon as possible:

1) **Improve and increase regulatory flexibility for low-risk Veterinary Health Products (VHPs) and feed additives by:**
    a. **Increasing the range of efficacy and prevention claims permitted on the label of feed and water additives and VHP's intended for use in food-producing animals (e.g. positive effects on pathogens and diseases);**
    b. **Permitting the use of individual VHPs in combination with other VHPs;**
    c. **Establishing a system to allow feed and water additives and VHPs approved in trusted jurisdictions to be allowed for use in Canada (e.g. Bill C-359);**
    d. **Institute changes to improve regulatory performance to more closely match stated performance targets.**

Identifying Barriers and Proposed Solutions: Veterinary Biologics (e.g. Vaccines, Diagnostic Tests)

Veterinary Biologics are regulated by the CFIA. The use of biologics, such as vaccines and diagnostic tests, are key strategies in the control and prevention of infectious diseases. Prevention of infectious disease, in turn, is a key strategy in antimicrobial stewardship.

Many vaccines used in food-producing animals in Canada were originally developed and marketed in either the US or the EU, each of which have their own distinct approval processes. As with pharmaceuticals, access to biologics, such as vaccines for use in food-producing animals, is also impacted by the potential for sales in the relatively small Canadian farmed animal industries.

Because Canada has attained such high health status for its farmed animal species, access to biologics from other countries must be controlled. These regulatory limitations are completely understandable because they protect the health status of Canadian livestock (e.g. testing for the presence of Bluetongue virus in imported attenuated vaccines), but others can present barriers that are more difficult to understand and justify.

One example is the current inability to import inactivated/killed vaccines that are only conditionally approved in the US[6]; Canadian regulations make it difficult, if not impossible, to readily import vaccines that are conditionally rather than fully approved in the US. This is frustrating for animal health companies, veterinarians, and producers because there are often no alternative vaccines available in Canada. One long-standing specific example in food animals is the vaccine to protect against *Clostridium perfringens* type A enteritis in cattle. This disease is virtually untreatable and often occurs in outbreaks that affect multiple animals. A vaccine has been conditionally approved in the US for some years – but cannot be similarly approved or easily imported into Canada. The reason this vaccine is only conditionally approved in the US is because there is no known way to recreate *Clostridium perfringens* type A enteritis itself – an essential step in satisfying regulators in the US that the vaccine is fully effective. Conditional effectiveness has been shown by the ability of the vaccine to induce an appropriate antibody response in vaccinated cattle. A system to facilitate matching conditional approval in Canada (or a similar mechanism) is likely to make it easier to maintain inventory of conditionally licensed biologics in Canada.

Another issue affecting access to vaccines is the limitations on the use of autogenous vaccines in Canada. Diagnostic capabilities have now developed to the point where veterinarians in certain food-producing commodities can precisely monitor microbial exposure of animals under their care. Veterinarians can then use this knowledge to generate specific, tailored disease prevention tactics that target the pathogens that were detected. One of those tactics is to create customized autogenous vaccines that contain the major pathogens found to be present on the farms under their care. These autogenous vaccines are referred to as 'prescription vaccines'.

As diagnostic technology advances even further, it will become even easier to monitor for the presence of specific microbes. This will fuel a further desire to develop and use autogenous vaccines especially in integrated food-production systems such as swine and poultry. Current regulations limit how such autogenous vaccines can be used. It should be possible to modify restrictions on the use of autogenous vaccines, provided the changes do not increase risks associated with their use.

Proposed Solutions: Veterinary Biologics

In order to address these barriers, our organizations strongly recommend implementing the following solutions as soon as possible:

1) **Create a process where inactivated vaccines that are conditionally approved in the US can be evaluated and similarly approved in Canada.**

2) **Re-evaluate restrictions on the use of autogenous vaccines, with a view to increasing the flexibility of their use within animal production system while still mitigating any risks.**

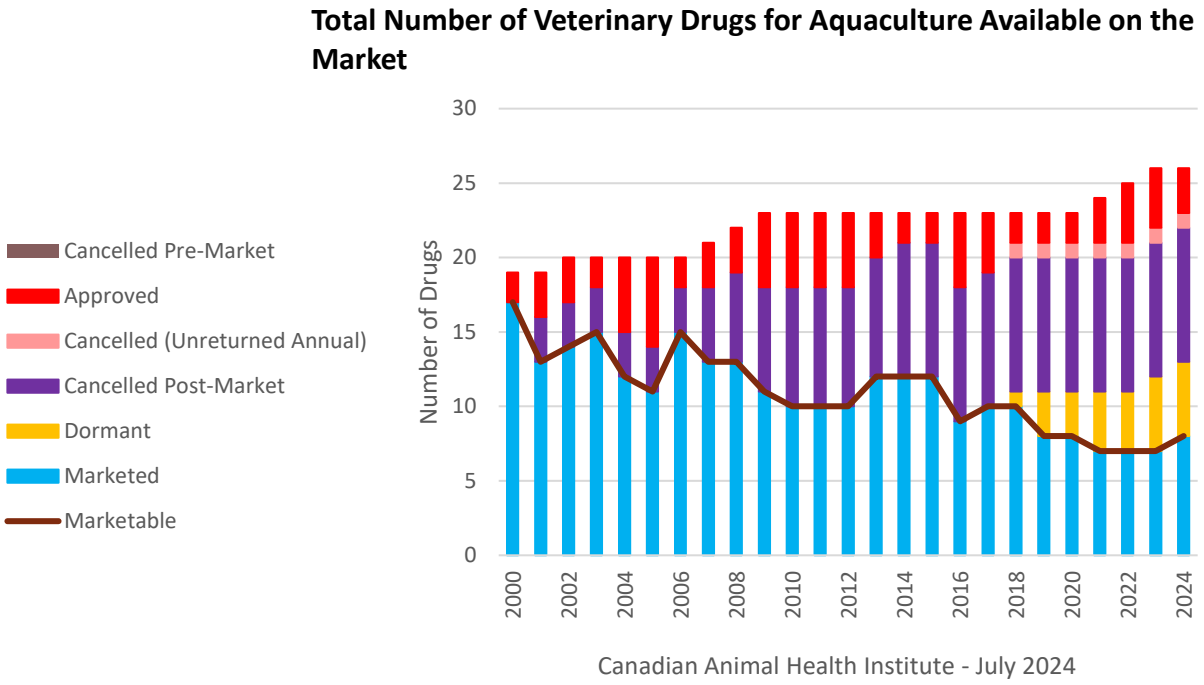
[6] Vaccines that are conditionally approved in the US have undergone the same purity and safety evaluations as fully approved vaccines but typically lack complete evidence of effectiveness.

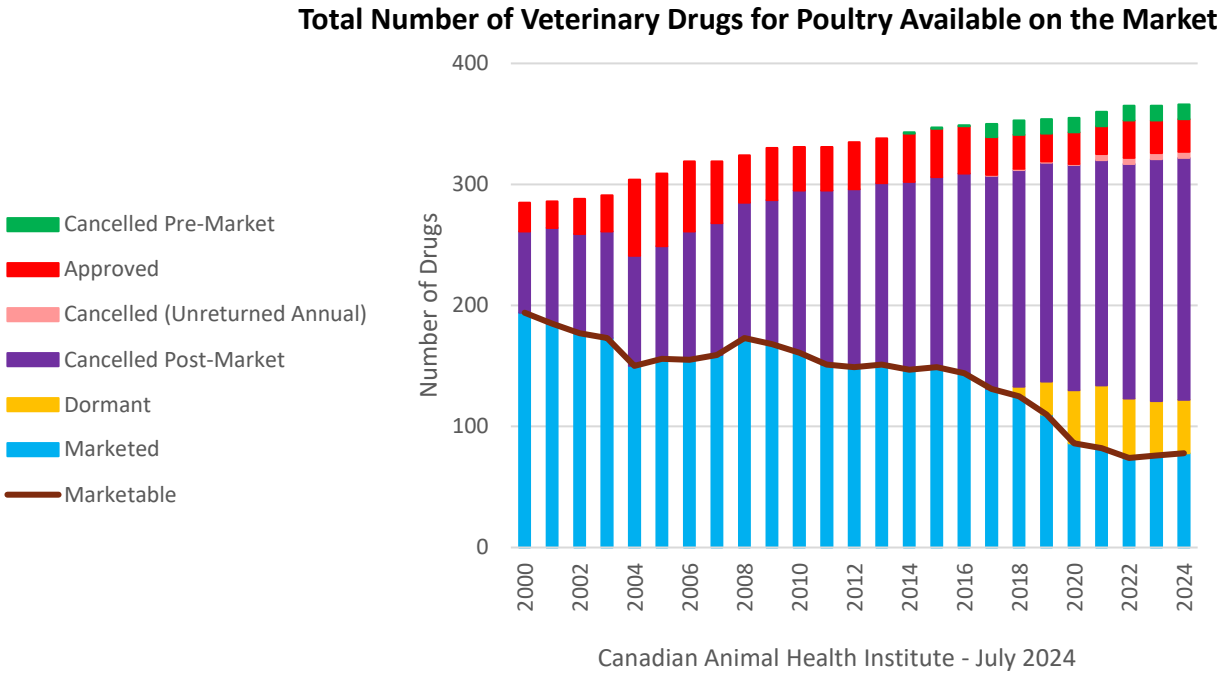
Conclusion

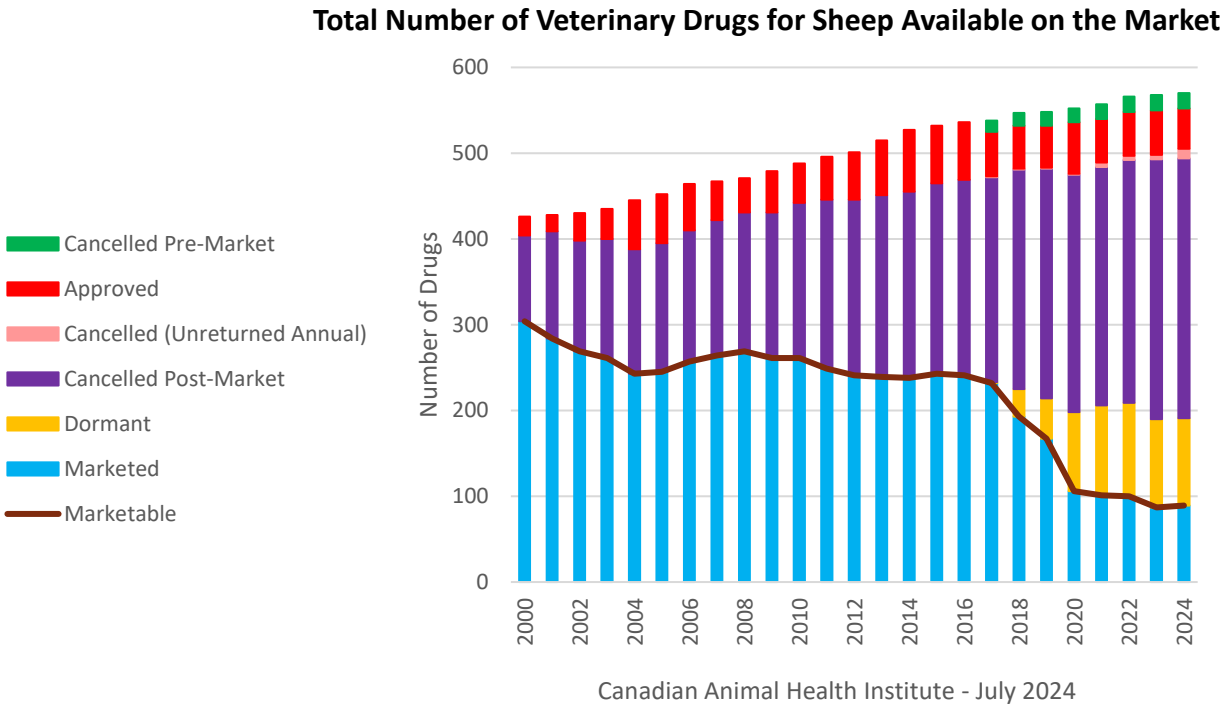
In order for Canadian producers to play their part in a One Health approach, they must be provided with access to additional and varied tools that will prevent and control illness and promote the health and wellbeing of animals.

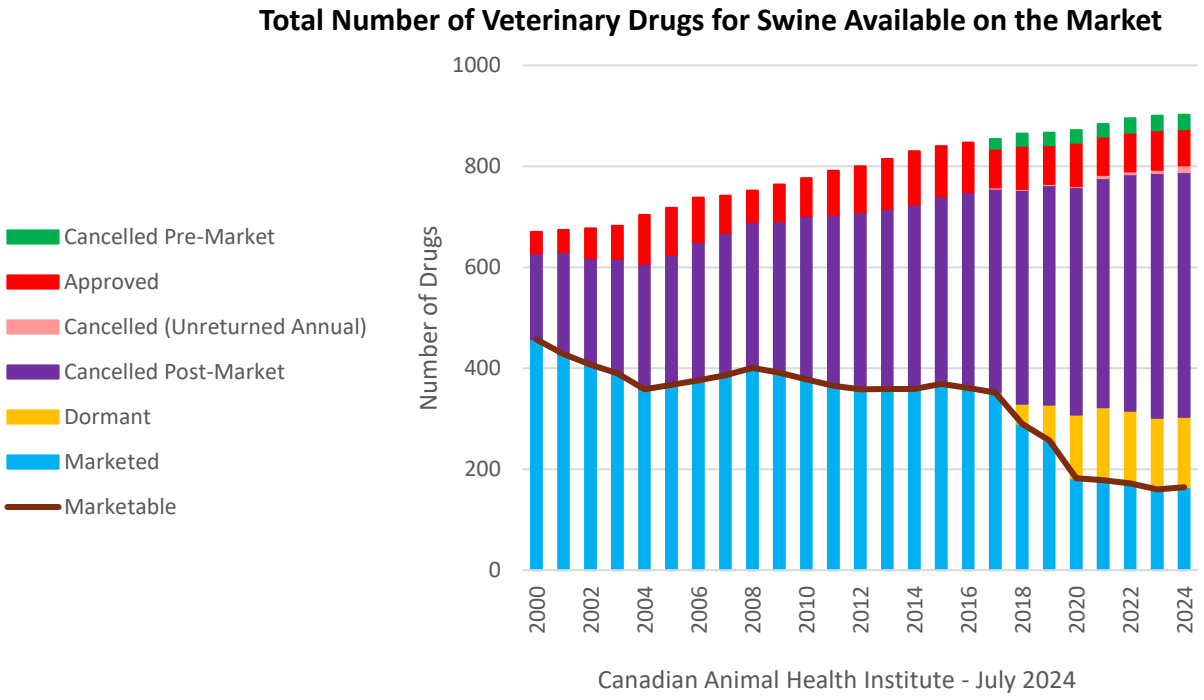
Our organizations, representing Canada's farmers, veterinarians, veterinary pharmaceutical and alternative product manufacturers, and feed providers strongly endorse the solutions outlined in this document – and ask the Government of Canada to take urgent action to address these complex issues.

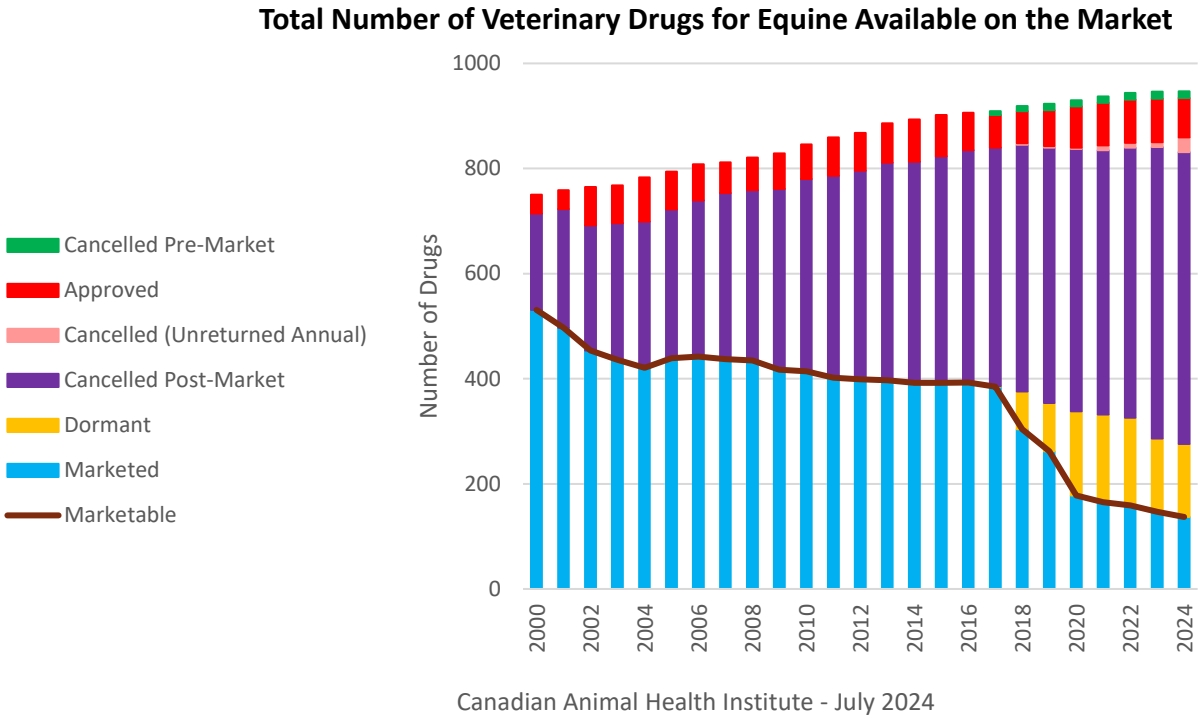
Appendix I – Total Number of Veterinary Drugs Available by Commodity




Total Number of Veterinary Drugs for Poultry Available on the Market
Cancelled Pre-Market
Approved
Cancelled (Unreturned Annual)
Cancelled Post-Market
Dormant
Marketed
Marketable
Number of Drugs
400
300
200
100
0
2000
2002
2004
2006
2008
2010
2012
2014
2016
2018
2020
2022
2024
Canadian Animal Health Institute - July 2024


Total Number of Veterinary Drugs for Sheep Available on the Market
Cancelled Pre-Market
Approved
Cancelled (Unreturned Annual)
Cancelled Post-Market
Dormant
Marketed
Marketable
Number of Drugs
600
500
400
300
200
100
0
2000
2002
2004
2006
2008
2010
2012
2014
2016
2018
2020
2022
2024
Canadian Animal Health Institute - July 2024


Total Number of Veterinary Drugs for Swine Available on the Market
Cancelled Pre-Market
Approved
Cancelled (Unreturned Annual)
Cancelled Post-Market
Dormant
Marketed
Marketable
Number of Drugs
1000
800
600
400
200
0
2000
2002
2004
2006
2008
2010
2012
2014
2016
2018
2020
2022
2024
Canadian Animal Health Institute - July 2024


Total Number of Veterinary Drugs for Equine Available on the Market
Cancelled Pre-Market
Approved
Cancelled (Unreturned Annual)
Cancelled Post-Market
Dormant
Marketed
Marketable
Number of Drugs
1000
800
600
400
200
0
2000
2002
2004
2006
2008
2010
2012
2014
2016
2018
2020
2022
2024
Canadian Animal Health Institute - July 2024

Appendix II – Logos of Organizations Jointly Endorsing this Document (Alphabetical)