Use of Antibiotics in

BC Livestock and Poultry Feed

2002 – 2021

Brian R Radke DVM PhD

Public Health Veterinarian

Office of the Chief Veterinarian

BC Ministry of Agriculture and Food

brian.radke@gov.bc.ca

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Preamble

The BC Ministry of Agriculture attended the Antimicrobial Stewardship in Canadian Agriculture and Veterinary Medicine Conference: How is Canada doing and what still needs to be done?[1], held October 30 to November 2, 2011 in Toronto. A reoccurring theme of the conference was the need for more monitoring of antibiotic use (AMU) in animals. It was recognized at the conference that the BC Ministry of Agriculture's information on aquaculture's use of antibiotics was one of the few existing sources of animal AMU data in Canada. Following the conference, the Ministry reviewed and analyzed its other AMU data available from its Veterinary Drug legislation and produced reports on the Use of Over-the-Counter Antibiotics in BC Livestock and Poultry[2]. The final report spanned 2002 – 2018. In 2018, federal animal antibiotic regulatory changes restricted the sale of animal antibiotics under the BC Veterinary Drug legislation to only feed mills. Therefore, the prior report was revised to include only antibiotics included in feed and data from 2019 to 2021 was added to result in the current report. The goal of the Ministry's AMU reports are to present and analyze the animal AMU information with full transparency.

Summary

This report analyzes the annual purchases of veterinary antibiotics by licensed commercial feed mills for inclusion in livestock and poultry feed 2002 to 2021. The purchase data is combined with product label information including active antibiotic ingredient concentration, approved animal species, and usage category (therapeutic, disease prevention, or growth promotion) and also incorporates Health Canada's categorization of antimicrobial class based on importance in human medicine. Antibiotic use is measured on a steady state biomass basis (gm of active antibiotic ingredient/tonne of steady state livestock biomass).

Some of the report's key findings include:

- Over the 20 year span from 2002 to 2021, total antibiotic use, on a population biomass basis, has fluctuated. It peaked in 2008, and then trended downward to 2014 resulting in usage less than 2002. The amount of antibiotics increased in 2016 to surpass the 2002 level, before decreasing in 2017 and 2018. The overall 20 year change is a 2.7% decrease.
- Federal regulatory changes with respect to animal antibiotics were implemented in 2018. BC total in-feed antibiotic use for livestock and poultry fluctuated from 2017 to 2021, decreasing 10.7% over this time. Since 2017, use of category IV antibiotics, which aren't important to human medicine, decreased 19% and mirrored the fluctuations in total in-feed usage. Category III products which are medium importance to human medicine increased 37% in BC feed from 2017 to 2021. The use of category II products, high importance in human medicine, decreased 95% from 2017 to 2021. The increased use of category III products offset the decrease in category II products. There has been zero use of category I, highest importance in human medicine, antibiotics in BC feed because such use has never been permitted in Canada, unlike Europe which historically (avoparcin) and currently (colistin) permits such use. Use of antibiotics in BC feed which are not categorized by Health Canada for importance in human medicine has been small and relatively constant.

- As of 2019, only category IV antibiotics can be used for growth promotion. These antibiotics are not important to human medicine because they are not used in human medicine.
- The federal ban on the use of medically important antibiotics as growth promotants resulted in an 8.2% decrease in category III antibiotics and a 6.8% decrease of category II products from 2017 levels. These respectively equate to a 5.9% and 2.0% decrease in the total amount of medically important antibiotics used in BC feed in 2017. The Canadian Antimicrobial Resistance Surveillance System and CIPARS report that from 2015 to 2018 annual use of medically important antibiotics in broiler and turkey flocks was less than 1% of their antibiotic use, while it varied from 26% to 12% in swine herds. They also report growth promotion use of medically important antibiotics continued in a small proportion of swine herds from 2019 to 2021.
- Ninety-five percent of the in-feed antibiotics used in 2021 had more than one label usage.
- Over three-quarters of the in-feed antibiotics used in 2021 were labelled for more than one animal species.
- The poultry industries' voluntary ban on the preventive use of category II antibiotics is estimated to have reduced category II use by 88% from 2017 levels which is a 25% reduction in use of medically important antibiotics in BC feed.
- Prior to 2018, the vast majority of in-feed medically important antibiotics did not require a prescription to be sold or purchased. There was no detectable effect in the BC in-feed AMU data from the federal 2018 requirement for a veterinary prescription in order to buy or sell these medicated feeds.
- The loss of BC non-feed AMU data was a foreseeable consequence the 2018 federal prescription requirement because the requirement meant BC's Veterinary Drug licensees could no longer sell the products, and veterinarians and pharmacists, who are able to sell the products, are not required to report their sales.
- As exemplified in this report, detailed AMU data is required to evaluate the appropriateness of that use and the effects of policy changes. The federal 2018 AMU regulatory changes required mandatory reporting of antibiotic sales for animals by manufacturers, importers and compounders. This included reporting by animal species and province. Yet the federal Veterinary Antimicrobial Sales Reporting (VASR) system has publicly reported only highly aggregated AMU data, that is less detailed than the AMU data the Canadian manufacturers of animal health products voluntarily provided prior to mandatory reporting. The loss of detailed antibiotic reporting by province for AMU of individual animal species is an unintended and unexpected result of the 2018 federal animal AMU regulatory changes.

Introduction

The primary scientific concern with AMU in animals is with the development of resistance to the antibiotics. Although the resulting antibiotic resistance (AMR) is a concern for animal health; the primary worry is the AMR could result in more AMR in human infections which could have negative implications for treatment of those infections. Debate continues as to the respective contributions of human AMU and animal AMU to AMR among human infections. A general, but not universal, consensus is that antibiotic use in humans is the main force behind development of antibiotic resistance impacting humans[3]. This does not mean interspecies transmission of resistance by bacteria isn't important. Transmission of bacterial resistance from animals to humans is an important concern. Similarly, transmission or resistance from humans to animals is also a concern. The AMU results in this report are then largely presented from a public health, as opposed to an animal health, perspective.

The report begins with a review of the legislative basis for the sale of animal antibiotics with and without a prescription, including the federal legislative changes effective December 1, 2018 that severely limited sales of the latter. This is followed by a description of the AMU data including the source of the data and the calculation of animal biomass. The results begin with comparing antibiotic use and animal biomass, before comparing 2 measures of annual AMU: 1) AMU mass; and 2) AMU mass on a biomass basis. AMU categorized by importance in human medicine is presented before separately reviewing annual AMU of category IV, III and II products. Where the BC feed data permits, the effect of the federal legislative changes on use of animal antibiotics is included in the discussion of the importance to human use categories. Categorization of AMU by importance in veterinary medicine is then considered. This is followed by the label usage category, and species label use. Then the need for caution in assessing the AMU results and their fluctuations is discussed. Finally, additional external data sources on animal AMU are reviewed in the context of the BC feed data to further assess the reasons for the reasons for the 95% decrease in category II use since 2017 including the role of the federal regulatory changes.

The legislative basis for the sale of antibiotics for use in animals with or without a prescription

Health Canada's Drug Product Database[4] includes all drug products approved for sale in Canada by the federal government. The Database includes products for use in humans and animals, it also includes prescription and non-prescription products. The federal government's Prescription Drug List[5] contains the pharmaceutical products, including antibiotics, which require a prescription in order to be sold. The List consists of two parts: Products for Human Use and Products for Veterinary Use. The latter requires a prescription from a registered veterinarian to be sold. The federal Feeds Regulations' Compendium of Medicating Ingredients Brochures[6] (CMIB) lists the medicating ingredients, including antibiotics, which can be added to livestock feeds (including feed for poultry and aquaculture). The Compendium specifies whether a veterinary prescription is required, the species of livestock, the level of medication, the directions for feeding and the purpose for which each medicating ingredient may be used, as well as the brand of each medicating ingredient that is approved for use in Canada.

Concerns that AMR is a complex and evolving public health issue motivated a number of changes in veterinary antibiotics in 2018 by the federal government. These changes included, as of February 2018, veterinary pharmaceutical companies' voluntarily removed growth promotion or production enhancement claims from labels of medically important antibiotics[7]. Medically important antibiotics are Category I - Very High Importance, Category II – High Importance, and Category III – Medium Importance antibiotics on Health Canada's 2009 Categorization of Antimicrobial Drugs Based on Importance in Human Medicine[8]. The deadline for ceasing the use of medically important antibiotics as growth promoters or production enhancers was December 1, 2018. Non-medically important antibiotics (Category IV – Low Importance), such as the ionophores and flavophospholipols, can continue to be used in feed for growth promotion or production enhancement. The federal government considers having appropriate veterinary oversight to be a key measure to promote the prudent use of antibiotics and minimizing the development and spread of AMR. Effective December 1, 2018, the federal government added most medically important veterinary antibiotics to the Prescription Drug List[7]. This applied to all dosage forms (that is, all methods of administration) of the affected antibiotics. Medications sold without a prescription are commonly referred to as over-the-counter (OTC) products. As of December 1, 2018 the only veterinary antibiotics which don't require a veterinary prescription and are available OTC are: antibiotics in the nitrofuran class of antibiotics which are applied topically; ionophores and flavophospholipols (bambermycin) which are administered in feed. Nitrofurans are Category III - Medium Importance in human medicine and includes four active ingredients. Nitrofurazone, and nitrofurantoin are the two active ingredients historically sold by BC Veterinary Drug licensees. The ionophores and flavophospholipols are Category IV - Low Importance to human medicine. The federal regulatory changes also limited personal use importation of veterinary drugs[9]. Mandatory reporting by manufacturers, importers and compounders on the sales of medically important antimicrobials for veterinary use was also required[10].

The Drug Schedules Regulation[11] of BC's Pharmacy Operations and Drug Scheduling Act notes which drugs, including antibiotics, can be sold without a prescription for use in animals. Provincial legislation must be consistent with the federal Prescription Drug List, with the option of requiring prescriptions for products not listed on the federal List. The BC Veterinary Drug and Medicated Feed Regulation[12] requires the manufacture and sale of medicated feed to comply with the requirements of the CMIB, including any requirement for a prescription.

The BC Ministry of Agriculture issues licences under the BC Veterinary Drugs Act[13] and Veterinary Drug and Medicated Feed Regulation for the sale of veterinary drugs. The classes of licence are: 1) medicated feed for the manufacture and sale of medicated feeds; 2) limited medicated feed for the sale, but not manufacture, of medicated feeds; and 3) veterinary drug for the sale of non-feed products containing veterinary medications including products that are injectable, water soluble, oral, topical, intrauterine, and intramammary. The BC legislation also licenses veterinary drug dispensers. A licensed dispenser is required to be present when medicated feeds are being manufactured and when a veterinary drug licensee is open for business. Pharmacies and veterinarians can also sell prescription and OTC veterinary drugs and are exempt from the BC Veterinary Drugs legislation licensing requirements. Commercial feed mills are considered wholesale druggists under the federal Food and Drugs Regulations, which allows them to import and buy prescription drugs. Medicated feed licensees can manufacture and sell prescription feeds as ordered by a registered veterinarian via a prescription. Limited medicated feed licensees and veterinary drug licensees are only permitted to sell OTC products, that is they cannot sell feed containing pharmaceuticals that require a veterinary prescription. As a condition of licensing, medicated feed licensees and veterinary drug licensees annually submit veterinary drug purchase records to the Ministry. The purchase records include the date of purchase, name of the supplier, quantity purchased, the generic name, trade name and name of the manufacturer of the drug.

A report on the Use of Over-the-Counter Antibiotics in BC Livestock and Poultry, 2002-2018 is available[2]. Updating of that report has been discontinued and is replaced by this report of in-feed annual antibiotic sales, prescription and OTC, by BC medicated feed licensees. Historically over 90% of the mass of OTC antibiotics were administered in feed and the remainder were administered via non-feed methods such as in water, topically or injected, etc. Antibiotics in the class nitrofurans are the only OTC products that is not administered in feed that the BC veterinary drug licensees can continue to sell after 2018. Historically, nitrofurans accounted for 0.001% of the total active antibiotic ingredients sold by licensees and in 2018 amounted to 0.19 kg of active ingredient. The nitrofuran OTC products are labelled for companion animals including horses and banned from use in food-producing animals[14].

Methods

Antibiotic Usage – The annual purchase records of medicated feed licensees and veterinary drug licensees are reviewed and antibiotic purchases of medicated feed licensees are entered into an Excel spreadsheet. The spreadsheet contains data from 2002 to 2021. Part of the 2006 purchase record of at least one medicated feed licensee is missing so antibiotic usage in that year is underestimated and must be interpreted with caution. The spreadsheet also contains veterinary product label information including: active antibiotic ingredient concentration, animal species, administration method and usage category (therapeutic, disease prevention, or growth promotion). In addition, the spreadsheet contains information on the antibiotic class of the active antibiotic ingredient, Health Canada's 2009 Categorization of Antimicrobial Drugs Based on Importance in Human Medicine[8] and the World Organization for Animal Health's (previously known as the OIE) categorization of antibiotics based on importance in veterinary medicine[15]. Antibiotic use by BC aquaculture is excluded from this analysis because that usage is reported by prescription which provides increased detail about the AMU and has been previously reported[16].

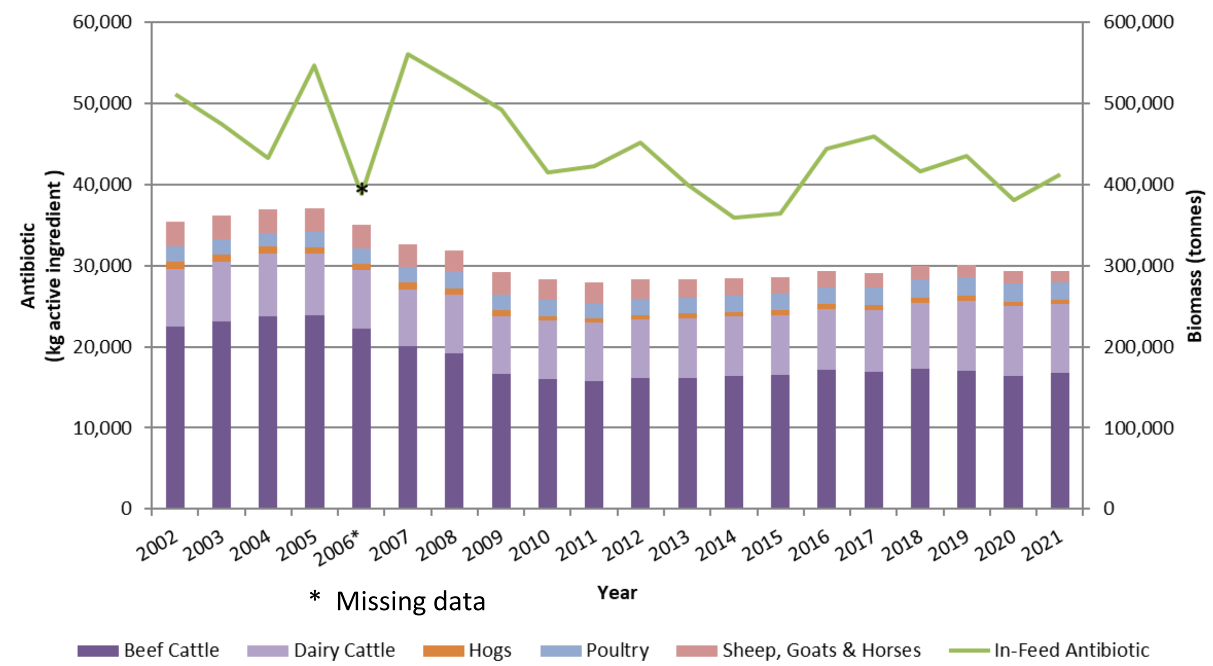
In summary, the BC Ministry in-feed antibiotic data includes purchases of veterinary antibiotics by licensed BC feed mills for inclusion in BC livestock and poultry feed. It includes prescription and OTC antibiotic products used in-feed, and is expected to be a comprehensive survey of in-feed use in BC livestock and poultry. In-feed antibiotics produced outside BC and shipped to BC producers from Alberta or producers that generate their own feed using on farm feed mills would not be captured in this data, but these sources of feed are rare in BC. Feed mills' purchases are expected to closely reflect sales; however, the two can vary based on changes in inventory between the beginning and end of a year.

Biomass – The annual steady state biomass of the following agricultural livestock commodities is calculated: beef cattle, dairy cattle, poultry (broilers, layers, broiler breeders, and turkeys), hogs, sheep, goats, and horses. The resulting steady state biomass estimates the total weight of BC livestock averaged over a year, that is, the biomass for an average day in the year. Technically, the biomass measure used is Adjusted Population Correction Unit[17]. The biomass is calculated using a variety of data sources including Statistics Canada Census of Agriculture data, livestock commodity group data and Agriculture and Agri-Food Canada slaughter data. Briefly, the calculation for a given commodity includes the estimated number, weights and lifetimes of the various production classes. Typically, both breeding livestock and slaughter animals are included for a given commodity. The biomass calculation considers how many days in a year a given type of animal is alive and any weight change during that time is also considered. An animal's steady state mass is the product of its average mass and the portion of the year it is alive. A broiler chicken is an example of a slaughter animal. A broiler chicken that hatches at 0.04 kg and over the span of 35 days grows to its slaughter weight of 1.98 kg has an average mass of 1.01 kg = (0.04 kg+1.98 kg)/2 over its lifespan of 0.096 = (35/365) of a year. So a broiler's steady state mass is 0.097 kg = 1.01 kg x 0.096. (For simplicity, the units of the steady state biomass are noted as mass; however, more accurately the measure is a density function with units mass·time.) In contrast, breeding livestock are typically animals which have finished growing and achieved a constant mature mass. For example, a beef cow has a constant mass of 590 kg for the entire year and therefore has a steady state mass of 590 kg = ((590 kg +590 kg)/2)*(365/365). So the combined steady state mass of 1 broiler and 1 cow is 590.097 kg = is 0.097 kg + 590 kg. Where growth curves are readily available, the area under the curve is integrated to determine the average mass of an animal, instead of using the arithmetic mean of a beginning and ending mass.

Results

Figure 1 shows the total mass of in-feed antibiotic active ingredient (AI) per year and the commodity composition of total biomass. The line in figure 1 is the total amount of antibiotics. Also, as noted in the figure and discussed in the Methods, the AMU in 2006 is underestimated due to missing records.

Figure 1. In-feed Antibiotic Use and Biomass
2002 - 2021



Total in-feed antibiotic use peaked in 2007, slightly surpassing usage in 2005. After 2007, total antibiotic use generally declined to 2014 when it reached the lowest point over the 15 years. Total in-feed antibiotic usage then increased from 2015 to 2017, then declined in 2018. Total in-feed antibiotic use increased in 2019, then decreased in 2020 and increased in 2021 to end slightly lower than the 2018 use.

The bars in figure 1 show the annual commodity composition of animal biomass. The total biomass fluctuates over the time period, peaking in 2005 and then declining until 2010. From 2010 to 2019 the biomass slowly rose, before slightly decreasing in 2020 and 2021. From 2007 to 2012 AI mass and biomass follow similar trends. After 2012 in-feed AI mass has fluctuated while the biomass has slowly risen. Over the period from 2012 to 2021 in feed antibiotic use has decreased by approximately 10%. The pattern of total biomass changes over the 20 years mirrors the beef biomass which is the largest contributor to the total biomass. The biomass of dairy cattle, which is the second largest contributor to total biomass, has slowly increased over the first 19 years, before declining slightly in 2021. The biomasses of hogs and especially sheep, goats and horses have declined over the 20 years. Overall, the poultry biomass has increased slightly over time; however, it declined in 2004 associated with BC outbreak of avian influenza. This outbreak resulted in a significant depopulation with cessation of production and importation of poultry products to replace the lost production.

The effect, if any, of the biomass' changing commodity composition on AMU is unclear.

Figure 2 compares total mass of in-feed AI with another measure of AMU. The light green line in figure 2 reproduces the total mass of in-feed AI line from figure 1. The second measure, the darker line, is in-feed antibiotic mass on a biomass basis, specifically gram of active ingredient per tonne of biomass. Figure 2 reveals the two measures of AMU are similar, with the biomass correction serving to dampen the fluctuations in AMU, especially in the first 10 years. For example, the mass of antibiotics is similar in 2005 and 2007. Yet AMU in 2007 is discernably greater than 2005 when measured on a biomass basis due to the larger 2005 biomass. Since 2010 the biomass has been relatively constant, so the two measures track similarly. In assessing antibiotic usage it is helpful to remove the effect of changes in the mass of the underlying animal population, and this is accomplished by measuring usage on a biomass basis. Such a population based measure is consistent with human AMU monitoring, although with humans the AMU denominator is typically population-days[18]. Hereafter, in-feed antibiotic use will be presented on a per biomass basis (gm of antibiotic active ingredient per tonne of steady state biomass measured as adjusted population correction unit).

Figure 2. Antibotic Use and Antibiotic Use on a Biomass Basis
In-feed
2002 - 2021

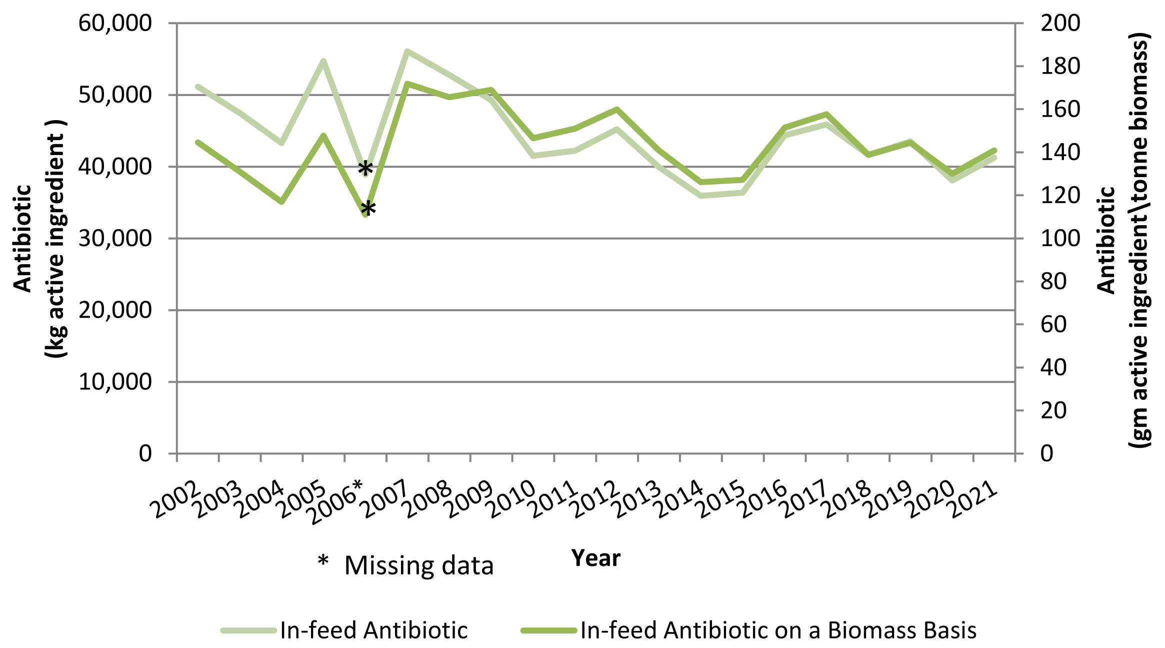
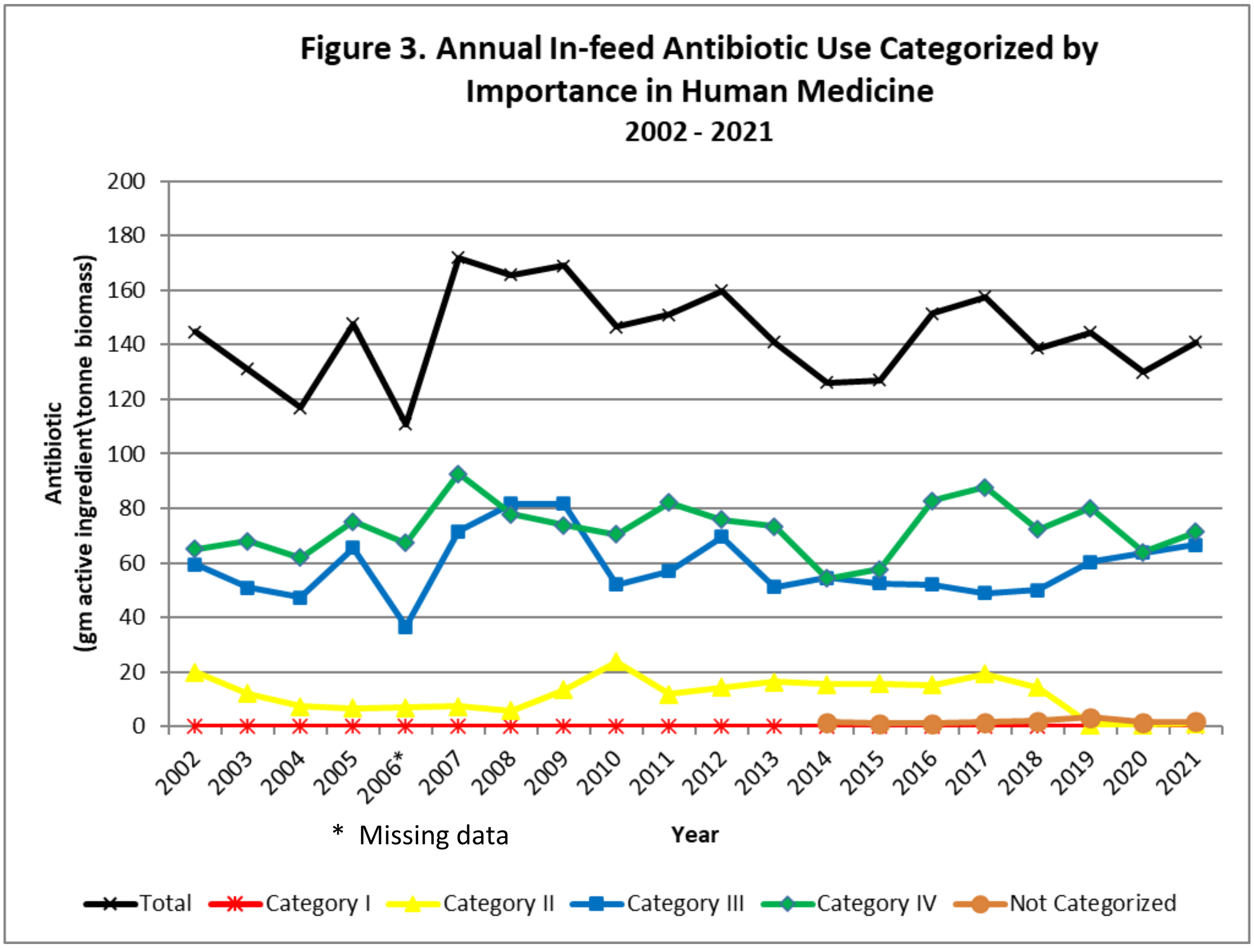


Figure 3 shows the annual antibiotic use categorized by Health Canada's importance in human medicine.



The data in Figure 3 is also presented in Table 1 in the Appendix. Over the 20 year span, total in-feed usage has changed from 145 gm of active antibiotic ingredient/tonne of biomass in 2002 to 141 gm of active ingredient/tonne of biomass in 2021, a 2.6% decrease. The peak antibiotic usage on a biomass basis occurred in 2007 at 172 gm/tonne of biomass. Total in-feed usage in 2017 was 158 gm/tonne of biomass, it decreased in 2018, increased slightly in 2019, decreased in 2020 before increasing to 141 gm/tonne of biomass in 2021, a 10.7% decrease from 2017.

There was no use of category I in BC feed throughout the 20 years, and a small amount of an in-feed antibiotic not categorized by Health Canada was used from 2014 to 2021. From 2017 to 2021 in-feed AMU of medically important antibiotics (categories I, II, and III) usage was 68 mg/tonne of biomass in 2017 and 2021, with a dip in the middle, for a net change of 0% over the four years.

Generally, the category of greatest use is IV which is considered not medically important by Health Canada because the ionophore and bambermycin antibiotics aren't used in human medicine. Annually, category IV products range from 43% to 61% of total in-feed AMU and averaged 51% over the 20 years. Category IV use peaks in 2007. Category IV usage rose substantially in 2016, and its decrease in 2018 accounts for the majority of decreased total use of antibiotics in 2018. From 2017 to 2021, category IV usage decreased 17 gm/tonne of biomass (19%) and followed a similar pattern of fluctuations to total usage.

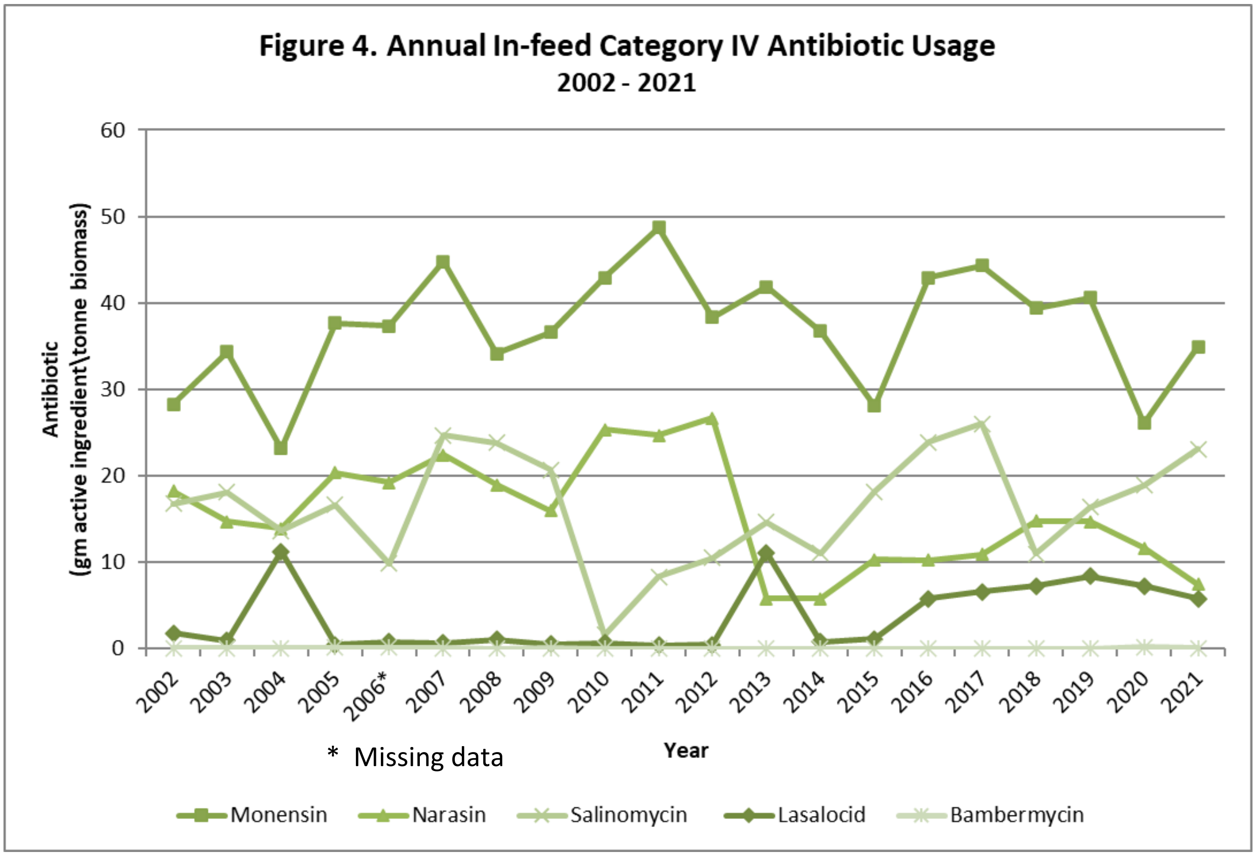
Annually, category III products which are of medium importance in human medicine, range from 31% to 49% of the total usage and average 41% over the 20 years. The use of category III products peaked in 2008 and thereafter has been trending down until 2018 when usage began constantly increasing through to 2021 (Table 1) resulting in an increase of 18 gm/tonne biomass (37%) since 2017.

The use of category II products, high importance in human medicine, is variable over time and peaked in 2010, and reached a lower peak of 19 mg/tonne of biomass 2017 before decreasing to 14 mg of active ingredient per tonne of biomass in 2018 and to approximately 1 gm/tonne biomass in 2019 to 2021, a 95% decline since 2017. Since 2017, the increase in category III usage has offset the decreases in category II AMU. Annually category II products range from 0.4% to 16% of the total usage (12% in 2017) and average 8% over the 20 years.

Unlike Europe, category I antibiotics have never been approved for use in-feed in Canada and therefore usage has been zero over the 20 years. Europe historically (avoparcin, antibiotic class glycopeptide) and currently (colistin, antibiotic class polymyxins) permits the use of category I antibiotics in feed[19].

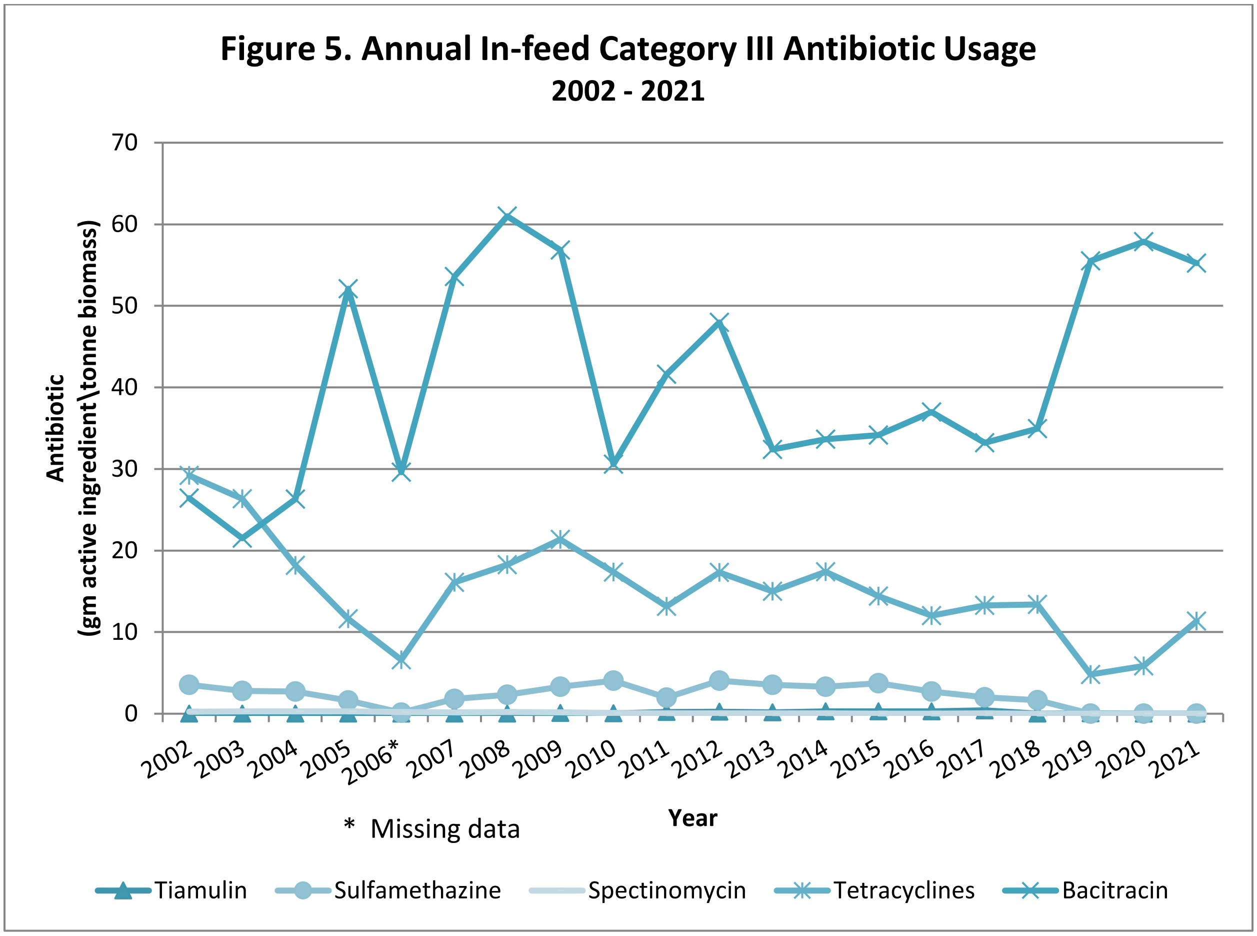
Avilamycin, from the antibiotic class orthosomycin, was approved as a prescription product in 2014 for use in broilers for the prevention of necrotic enteritis. It has not been categorized for importance to human health by Health Canada. This active ingredient and its class of antibiotics are not used in human medicine. Since its introduction, it's level of use in BC feed has been small and relatively constant (Table 1).

Figure 4 shows the usage of category IV antibiotic active ingredients in-feed over time. Table 2 (Appendix) reports the same information but in greater detail.



Category IV antibiotics are not used in human medicine and are available in-feed without a veterinary prescription. Health Canada considers category IV antibiotics to be of low importance in human health and not medically important, therefore, potential use of this category for growth promotion/production enhancement is permitted. Yet, the public health implications of ionophore use have been noted[20]. Monensin accounts for approximately half of the category IV usage followed by salinomycin, narasin and lasalocid. Monensin, narasin, salinomycin and lasalocid belong to the ionophore antibiotic class, and bambermycin belongs to the flavophospholipols class. Since 2018 and on a biomass basis, monensin and narasin use declined, salinomycin use increased, lasalocid use remained relatively constant, while bambermycin use increased slightly. Bambermycin is the only category IV antibiotic with only a growth promotion label. Its use has been very small over the 20 years (Table 2).

Figure 5 shows the usage of category III antibiotic active ingredients over time. Table 3 in the Appendix reports the same information but in greater detail.

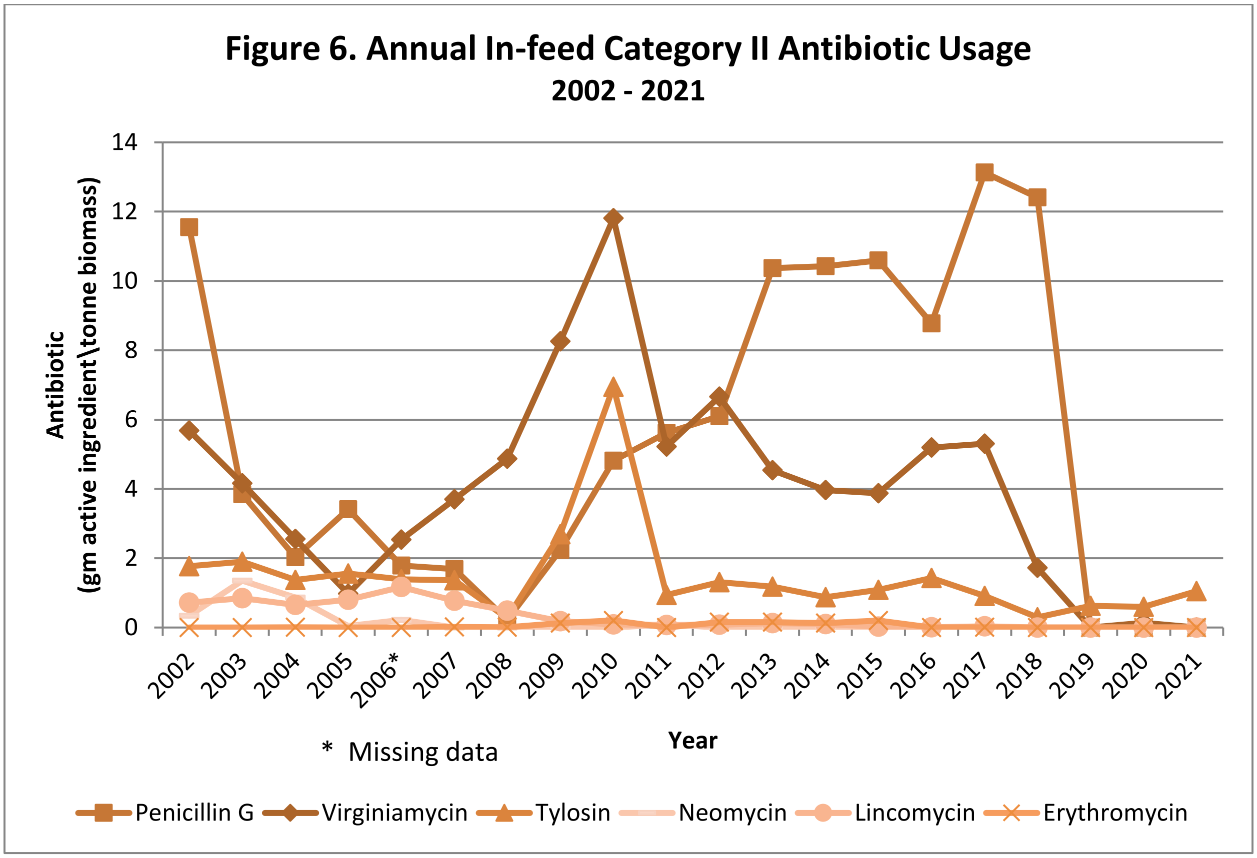


Health Canada considers category III antibiotics to be of medium importance in human medicine. Bacitracin usage fluctuates over the 20 years, particularly 2004 to 2013 and in 2019, and has accounted for over half of the category III usage. From 2018 to 2019 bacitracin use increased 59% and remained elevated in 2020 and 2021. This increase in bacitracin is responsible for the increased total category III usage in BC feed as of 2019. In 2017, the United States required prescriptions for most antibiotics administered in feed and water[21]. In the US, bacitracin is not considered medically important and it maintains its non-prescription status in that country[22]. Bacitracin is also available OTC in the human skin ointment Polysporin® which also contains polymyxin B, a category I critically important to human medicine antibiotic. Usage of the tetracycline class in BC feed also fluctuates. As of 2004, tetracycline is the category III antibiotic class with the second highest usage, and accounts for approximately 25% of the category's active ingredients over the 20 years. The antibiotics used in this class are chlortetracycline and oxytetracycline. Combined, bacitracin and tetracyclines account for over 90% of the annual category

III usage. Non-potentiated sulphonamides is the category III antibiotic class with the third highest level of usage, averaging approximately 4% over the 20 years. Usage of this class peaked in 2010 at 8% of the category III class usage. The use of spectinomycin and tiamulin (swine only) have been very small (<0.1 gm/tonne biomass) over the 20 years. Since 2017, category III usage has increased driven by a large increase in bacitracin use, while tetracycline use has fluctuated and use of spectinomycin and sulfamethazine ceased (Table 3).

The spectinomycin product also contained lincomycin, a category II antibiotic. Due to the timing of the cessation of this product's use it is tempting to associate this with the federal regulatory changes. Yet, the product wasn’t labelled for growth promotion and continued to be available after 2018 as a prescription product. Therefore, the ceasing of its use is not due to the ban on use of medically important antibiotics for growth promotion, although it could be due to its movement to the prescription drug list. In contrast, the sulfamethazine product was labelled solely for growth promotion in feedlot cattle so this product was banned from the market in 2018. This product contained equal amounts of tetracycline and in 2017 accounted for 2.01 gm tetracycline/tonne biomass, and other tetracycline containing products accounted for 11.27 gm tetracycline/tonne of biomass. This growth promotant accounted for 8.2% (4.02/48.97) of category III use in 2017. Many of the other tetracycline containing products had growth promotion label indications in combination with disease prevention or treatment indications and continued to be available after 2018 without the growth promotion indications. Tetracycline use decreased noticeably in 2019 and 2020 before increasing in 2021 to 11.36 gm/tonne of biomass which is similar to the 2017 level of use after removing the growth promotion product (11.27 gm/tonne biomass). This suggests the sizable decrease of tetracycline use in 2019 and 2020 were due to the random fluctuations in antibiotic use routinely observable in BC in-feed AMU, and not due the removal of the growth promotion use. Additional years of data can shed further light on such issues.

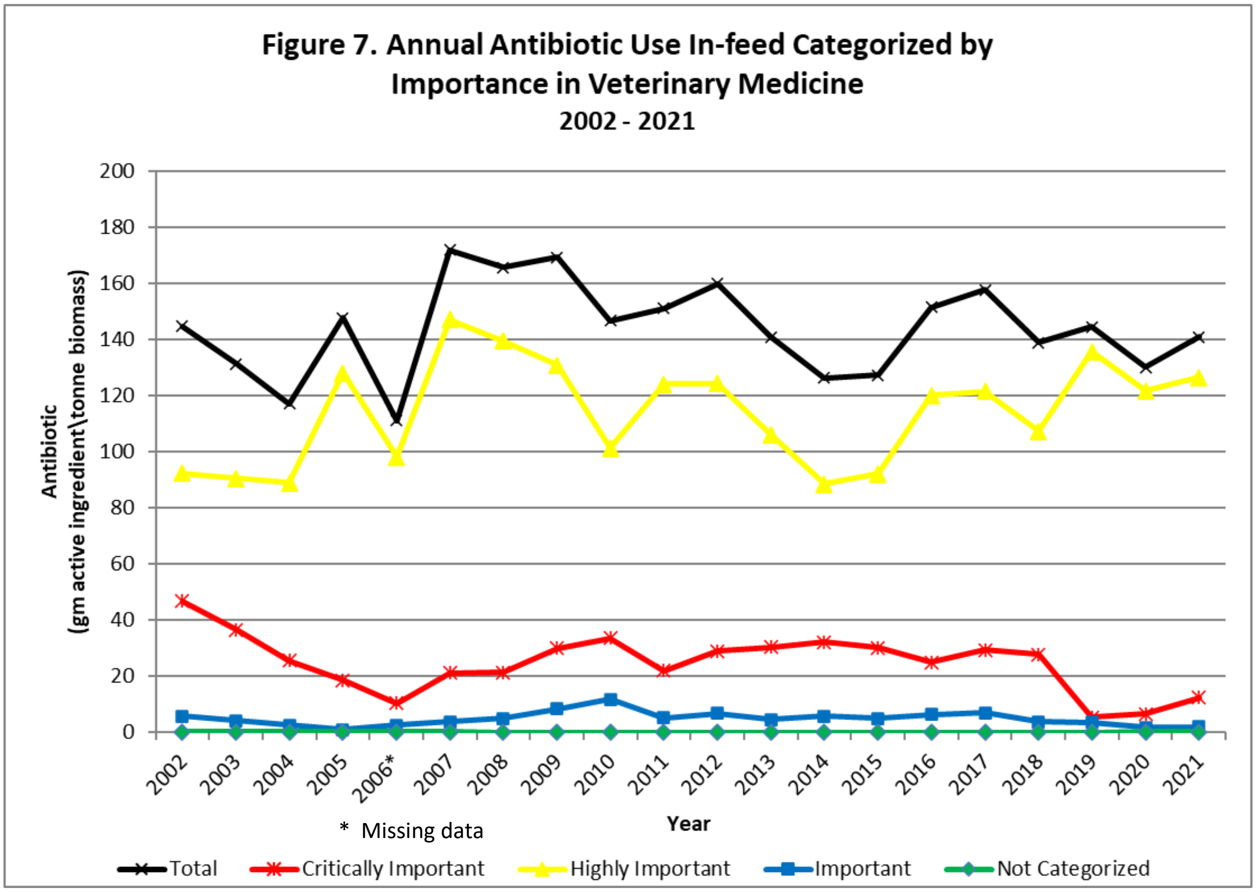
Figure 6 shows the in-feed usage of category II antibiotic active ingredients over time. Table 4 reports the same information but in greater detail.



Health Canada classifies category II antibiotics to be of high importance in human medicine. Prior to 2019, penicillin G and virginiamycin (streptogramin class) accounted for approximately 60 to 98% of the annual in-feed category II usage. Penicillin G use in-feed decreases from 2002 to 2008 and then rises from 2009 to 2017 with slight downturns in 2016 and 2018, and dropped precipitously to zero as of 2019. From 2002 to 2018, penicillin G averages 44% of annual category II usage in-feed, and averaged over 62% of the annual use from 2011 to 2018. Virginiamycin use increases from 2005 to a peak in 2010 when it accounted for 50% of the in-feed category II usage. Thereafter, virginiamycin use trends lower, including a marked decrease in 2018, with zero use in 2019 and 2021, and use of a small amount in 2020. Tylosin (macrolide class) use is relatively low over the twenty years except for 2009 and 2010 when it peaked. It was approximately 1 gm/tonne biomass or less from 2017 to 2021. Use of the remaining category II antibiotics has been low over the twenty years. This includes neomycin (aminoglycoside class), lincomycin (lincosamide class), and erythromycin (macrolide class). Their combined annual usage averaged 7% of the in-feed category II usage from 2002 to 2017, since 2018 their use has been zero. Since 2017, the 95% decrease in category II usage is primarily due to the 2019 cessation of penicillin G use and decreased use of virginiamycin. The penicillin and virginiamycin accounted for 72% and 28% of the 2017 category II antibiotic use in 2017. The 2018 cessation of the very small amounts of erythromycin and lincomycin use had minimal effect on the total category use.

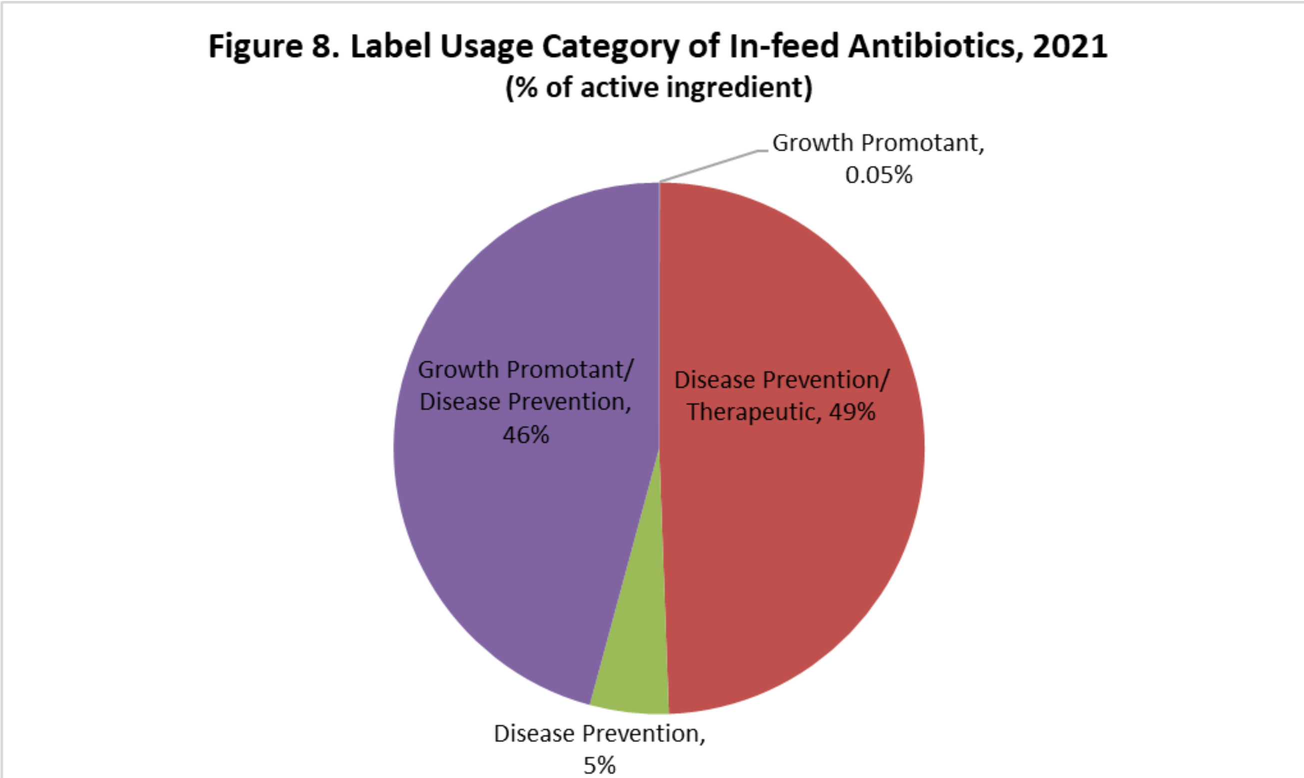
The erythromycin product was labelled for growth promotion in poultry and this product was removed from the market in 2018 due to the federal ban on the growth promotion use of medically important (category I to III) antibiotics. As noted, in the category III antibiotic discussion, the lincomycin was a combination product with spectinomycin and didn't have a growth promotion indication, so it's cessation of use as of 2018 was unrelated to the federal changes. The penicillin included in BC feed in 2017 and 2018 came from two feed additives both labelled solely for use in broilers. One additive accounted for 10% of the penicillin and was labelled for growth promotion, the other labelled as a treatment aid accounted for 90% of the penicillin. Following the regulatory change, latter product continues to be marketed while the former was discontinued. So although penicillin usage stopped after 2018, only 10% of the reduction is due to the ban on growth promotion. Prior to 2019, the tylosin product was labelled for treatment of broilers, for treatment or prevention or growth promotion of pigs, and for prevention in feedlot cattle. This product continued to be marketed after 2018 with the deletion of the hog growth promotion indication. Prior to 2019, virginiamycin was marketed for growth promotion or disease prevention in broilers, for growth promotion or disease treatment in hogs. After 2018, virginiamycin continued to be marketed without the growth promotion labels and with the addition of disease treatment of feedlot cattle. Combined the erythromycin and penicillin growth promotants amounted to 6.8% (1.32/19.38) of category II antibiotic use in 2017.

Figure 7 shows the categorization of antibiotic usage by their importance in veterinary medicine.



The World Organisation for Animal Health's (WOAH), previously known as the OIE, international categorization for importance of antibiotics in veterinary medicine is used as Canada does not have a national veterinary categorization system. Every year the majority of antibiotics used in BC feed are highly important in veterinary medicine, ranging from 64% to 94% of the total active ingredient on a biomass basis. The critically important antibiotics in veterinary medicine are consistently the second largest category, ranging from 4% to 32% of the total. Antibiotics important in veterinary medicine account for between 1% and 8% of usage annually. Bambermycin, which is considered not medically important in human medicine, is the only antibiotic active ingredient used in BC feed that isn't categorized by WOAH, and accounts for less then 1% of annual in-feed usage. In 2019, the use of critically important antibiotics decreased substantially, before increasing in 2020 and 2021. Since 2019, use of important antibiotics has decreased slightly, and use of highly important antibiotic in-feed has increased.

Figure 8 summarizes for 2021, the usage categories for in-feed antibiotic purchases based on the product labels.



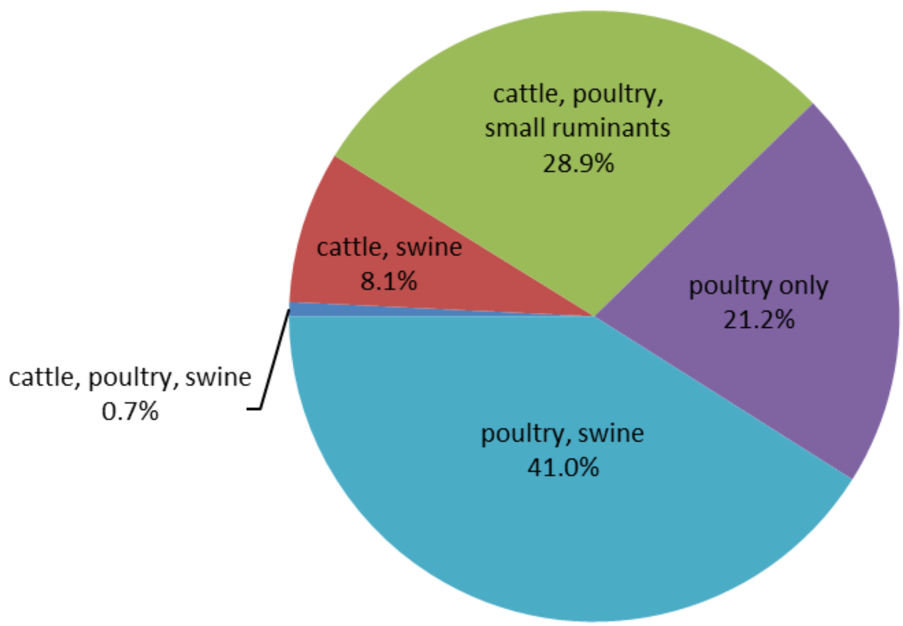
The three label usage categories for in-feed antibiotics are: therapeutic, disease prevention and growth promotant, with the latter being limited to category IV (not important in human medicine) products as of 2019. The majority of antibiotics used have more than one label usage category. For example, monensin, a category IV ionophore, is labelled as a growth promotant and for disease prevention. It and similarly labelled products account for 46% of the total active antibiotic ingredients used in 2021. In contrast, in 2018 prior to the ban on growth promotion use of medically important antibiotics, 79% of the antibiotics used included a growth promotion label indication[2]. Forty-nine percent of the 2021 antibiotic active ingredients used were labelled for disease prevention and/or therapeutic usage. Five percent of antibiotics used in-feed in 2021 were labelled solely for disease prevention. Bambermycin, a category IV antibiotic, was the only active ingredient used that was labelled only for growth promotion and accounted for less than one percent of the in-feed antibiotics administered in 2021.

The breakdown by labelled usage is consistent with the categorization of usage in Figure 3. All products labelled with a growth promotion indication are category IV, not medically important, products. Some category IV products have a single label usage: either growth promotion or disease prevention. All active ingredients labelled with disease prevention/therapeutic usage are category II or III as are the bulk of in-feed products labelled for disease prevention.

For products with more than one label usage, it is not possible to parse the usage into the different individual usage categories. Due to 95% of the active ingredients having labels with more than one label usage category, this data is not informative with respect to assessing antibiotic usage for therapy versus disease prevention versus growth promotion.

Figure 9 summarizes, for 2021, the combinations of species based on the product labels.

Figure 9. Species Label Use of In-feed Antibiotics, 2021
(% of active ingredient)



Approximately 21 percent of 2021 AMU in feed is labelled for use in a single species, 21.2% in poultry and less than 0.1% in swine (data not shown). The majority of products are labelled for use in more than one species. For example, monensin, a category IV ionophore, is labelled for use in cattle, poultry and small ruminants. That product and others similarly labelled account for 28.9% of active antibiotic ingredients purchased in 2021. Products labelled for use in poultry and swine accounted for 41.0% of the active ingredients. About 8 percent of the active ingredients in feed in 2021 were labelled for cattle and swine, with less than 1% for cattle, poultry and swine.

For products with more than one label species, it is not possible to parse usage among the species.

Caution in assessing usage amounts and their fluctuations

Incomplete 2006 purchase record data for at least one medicated feed licensee results in an underestimation of usage for that year and likely overstates the fluctuation in AMU. A less obvious potential source of annual AMU fluctuations are substituting between products that vary in dosage rate. For example, salinomycin, monensin, and narasin and are all category IV ionophores approved for coccidiosis prevention in broilers. For this label indication, salinomycin is included at a rate of 60 mg/kg of feed and monensin's inclusion rate is 99 mg/kg. Narasin's inclusion rate is 40 mg/kg for a combination product and 70 mg/kg when narasin is the only active ingredient. Substituting monensin for salinomycin in the prevention of broiler coccidiosis would result in a 65% increase in AMU.

AMU measures such as defined doses remove the effect of dosage rate[23]. Such measures require information on the species the product is being administered to, and therefore, can not be calculated with the current data. Steady state biomass, corrected for the animal species' lifespans, has been used to put the OTC AMU into a population context. The effect on usage and its fluctuations of changes in the commodity composition of the biomass is unknown.

AMU on a biomass basis also fluctuates due to changing disease dynamics as the diseases experienced by the different animal species and their appropriate treatments, including antibiotics, change over time.

The effect of the 2018 federal regulatory changes

Disappointingly, there doesn't appear to have been any evaluation, peer-reviewed or otherwise, of the federal regulatory changes which occurred 4 years ago. Evaluation is important to assess the outcome of the changes. Information on the effectiveness of such interventions can inform Canada or others on the future use of similar measures and to inform Canada's future antibiotic stewardship activities.

BC's in-feed AMU data, complemented by other data, will be used to evaluate the federal changes including movement of veterinary products with medically important antibiotics (category I to III importance to human medicine) to the prescription drug list and the removal of growth promotion label indications from in-feed veterinary products with category II and III antibiotics (Canada never had Category I products approved for use in feed, much less as growth promotants). In evaluating the changes, first the degree of implementation will be considered, followed by the effect of the change on AMU.

Review of the Drug purchase records of Veterinary Drug Licensees reveals, with two exceptions, all of the veterinary products with Category I to III antibiotics that were available over the counter were moved to the prescription drug list and therefore could no longer be sold by the Veterinary Drug or Limited Feed Licensees. Sales of prescription drugs are limited to veterinarians, pharmacists, and in the case of feed, feed mills. Products containing the category III antibiotics, nitrofurazone or nitrofurantoin, continue to be sold without a prescription. These are topical medications labelled only for companion animals. The human over-the-counter antibiotic skin ointment, Polysporin® contains antibiotics critically important to human medicine, and important to human medicine.

Removal of growth promotion label indications from veterinary products with medically important antibiotics (Category I to III) was confirmed by reviewing the label indications of those products included in BC feed livestock and poultry feed from 2019 to 2021. The not medically important Category IV products were the only active ingredients used in BC that included a label indication for growth promotion.

The impact of the growth promotion ban on AMU is less clear. As noted in the discussion of categories II and III usage, in 2017 products labelled solely for growth promotion in poultry accounted for 6.8% of the annual category II usage and those labelled solely for growth promotion in feedlot cattle accounted for 8.2% of the category III use in BC feed. Respectively, these growth promotion uses accounted for 2.0% and 5.9% of the total amount of medically important antibiotics used in 2017. These amounts are small; however, these results only consider products labelled solely for growth promotion. Historically, approximately 75% of the mass of medically important antibiotics included in BC feed had a label indication of growth promotion along with therapeutic and/or disease prevention. It's possible some of that mass was used for growth promotion, but this can't be determined from the BC in-feed data. Other Canadian AMU data can shed light on use of medically important antibiotics for growth promotion use before and after the ban.

The Canadian Antimicrobial Resistance Surveillance System (CARSS) Report 2021[24] includes indications for use in sentinel broiler chicken flocks, grower-finisher pig herds and turkey flocks. Figure 25, page 73 reports that from 2015 to 2018 growth promotant use in broiler flocks and turkey flocks consistently accounted for less than 1% of the total category I to III antibiotics used in those flocks. This low level of growth promotant use in poultry is consistent with the 6.8% of 2017 category II (penicillin and erythromycin) antibiotics identified in the BC in-feed AMU data as used for poultry growth promotion. Use of these products in the grower-finisher pig herds varied from 26% in 2015 to 12% in 2018. The use of medically important antibiotics for growth promotion was zero for the broiler and turkey flocks in 2019. However, CARSS reports three of the 107 sentinel grower-finisher pig herds used medically important antibiotics for growth promotion in 2019 and this accounted for 3.3% of their use in 2019. The Canadian Antimicrobial Resistance Surveillance System (CIPARS), who conducts the sentinel animal surveillance reported by CARSS, notes four sentinel grower-finisher pig herds reported using medically important antibiotics for growth promotion in 2020, although the doses and durations were consistent with labelled claims for disease treatment and/or prevention[25]. Notably, CIPARS in 2019 began sentinel antibiotic use surveillance in beef feedlot cattle and dairy cattle herds, and in 2020 began a pilot on egg laying chicken flocks. Then information on growth promotant use of medically important antibiotics in these animals prior to 2019 will not be available, and use since 2019 has not been included in reports generated to date. Caution is required in interpretation of the sentinel herd results as the herds are not a random sample – producers' and their veterinarians' participation is voluntary.

In summary, the very low amount of medically important antibiotics used in poultry growth promotion reported by CARSS and CIPARS is consistent with this report's findings of the erythromycin and penicillin use for growth promotion discussed in association with Figure 6. Not detecting use of medically important antibiotics in BC feed for hogs, although in contrast to the federal findings, is not surprising. The size of the provincial hog herd is small and has been declining over the last 20 years. In 2021, hogs accounted for less then 2% of BC's biomass. Both the absolute and relative size of BC's hog herd is much smaller than most other provinces. CIPARS' sentinel AMU surveillance farms are representative of the national distribution of the animal species. BC hog farms are not included in the sentinel program due to BC's small hog population relative to the prairies, Ontario and Quebec. (BC broiler flocks and turkey flocks are included in the poultry sentinel flocks surveillance.) Beef cattle account for over half of BC's livestock and poultry biomass (Figure 1), beef cows and calves are the vast majority of this biomass with feedlot animals accounting for less than 10% of the beef animal biomass. Then it is not surprising that use of category III products for growth promotion of feedlot cattle was relatively small at 4.02 mg/tonne of biomass which is 8.2% of that category's total use. No medically important antibiotics were historically approved for use in-feed of beef cows or calves, and furthermore, these animals are typically grazing and on range and fed little prepared feed. Similarly, no medically important antibiotics were historically approved for use in dairy animals which account for approximately one-quarter of BC's livestock and poultry biomass. The structure of the BC livestock and poultry industry helps explains the overall very low use of medically important antibiotics in feed for growth promotion prior to the federal ban.

As noted in the Figure 3 discussion, category II usage in BC feed decreased by approximately 95% after 2017 and remained very low to 2021. The ban on growth promotion accounted for 6.8% of the 2017 category II use, and it is worth evaluating whether the largest portion of the decrease could have been due to the regulatory changes, including the prescription requirement for medically important antibiotics. This evaluation involves considering federal sources of animal AMU data which is measured as mg of antibiotic/PCU, where PCU is measured in kilograms. However, the federal biomass calculation is not equivalent to the biomass indicator used in this report because different animal weights are used in the calculations and the federal indicator doesn't consider the length of the animals' lives. As a result, the reported federal mg/PCU are not directly equivalent to the AMU measure used in this report.

The most recent CIPARS detailed antibiotic use data in-feed from the sentinel farms is for 2019 and includes data by province[26]. None of the 34 sentinel broiler flocks in BC reported category II usage in-feed in 2019 while 53% and 7% reported use of penicillin and virginiamycin, respectively, in 2018. In 2017, broilers received 17 mg/PCU of penicillin and 12 mg/PCU virginiamycin, and in 2018 received 66 mg/PCU and 4 mg/PCU, respectively. Similarly, among the 31 sentinel turkey flocks in BC, category II usage in-feed in 2017 was 0 mg/PCU for penicillin and 17 mg/PCU for virginiamycin, and 2 mg/PCU and 23 mg/PCU respectively in 2018. Use in turkeys in 2019 was 0 mg/PCU for penicillin and 2 mg/PCU for virginiamycin. And this reduction of penicillin and virginiamycin use was consistent with use in the other provinces (e.g., Alberta, Saskatchewan, Ontario and Quebec) with sentinel broiler and turkey flocks. Although, Ontario and Quebec reported continued feed use of trimethoprim-sulfas, a category II product, in 2019. In contrast, the swine sentinel herds used smaller amounts of penicillin and virginiamycin in-feed in 2017, 3.7 mg/PCU and 1.6 mg/PCU, respectively, and in 2018, 1.6 mg/PCU and 0.7 mg/PCU, respectively and this decreased to 0.9 and 0.5 in 2019. Overall the amount of category II usage in the swine feed remained relatively constant from 2017 (50.4 mg/PCU) to 2018 (40.6 mg/PCU) to 2019 (40.3 mg/PCU). CIPARS also noted the continued precipitous decline in category II usage in 2021 among all methods of administration in broiler and turkey sentinel farms and much smaller declines of category II usage in grower-finisher pig herds[27].

The CIPARS BC sentinel poultry flock AMU data corroborates the finding in this report that the 2017 and 2018 penicillin purchases were labelled solely for poultry. The CIPARS data reveals in those years: BC poultry flocks also received virginiamycin; use of virginiamycin was less than penicillin in the flocks; and in 2019, use of penicillin was zero and virginiamycin use was drastically reduced. In contrast, use of these 2 category II antibiotics in the sentinel hog herds was an order of magnitude lower, and more constant from 2017 to 2019 than the poultry use. The pattern of penicillin use and virginiamycin use in BC feed from 2017 to 2019 (Table 4) is highly consistent with the pattern of use in the sentinel poultry flocks, strongly suggesting at a minimum, the majority of the virginiamycin in BC feed from 2017 to 2019 was fed to poultry and not swine. (Until 2019, virginiamycin feed antibiotics were labelled only for use in poultry or swine.) If use occurred in both species it is plausible that poultry use would drive the temporal pattern of use due to poultry's higher level of use and BC's poultry biomass being over 4 fold greater than the BC hog biomass. Moreover, the use of the virginiamycin was not for growth promotion in BC poultry because CARSS stated less than 1% of the in-feed antibiotics were use for growth promotion in and BC in-feed data identified that as a penicillin product. In summary, based on the BC in-feed data and CIPARS data, at a minimum, the bulk of the penicillin and the virginiamycin used in BC feed in 2017 and 2018 were not for growth promotion, and use of the two antibiotics was zero from 2019 to 2021, with the exception of 2020 when virginiamycin use was 2.5% of its 2017 level of use.

This dramatic and unique pattern of decreased use for these two category II drugs which were not being used for growth promotion, is consistent with Step 2 of the national poultry producer's Antimicrobial Use Strategy[28]. Step 2 was, as of January 1, 2019, Canadian broiler and turkey producers' voluntary elimination of the preventive use of Category II antibiotics. This followed their Step 1 elimination of Category I antibiotics for disease prevention. CIPARS has noted the AMU reduction resulting from the strategy[27]. The effectiveness of the poultry industry's AMU strategy in reducing AMU has been noted along with the suggestion that the strategy potentially resulted in increased frequency of infectious diseases, thereby increasing the need for AMU through water for disease treatment[29]. As noted in the discussion of Figure 5, bacitracin use increased 59% in 2019 and was responsible for the increased total use of category III products. Bacitracin in-feed is labelled for use solely in poultry and hogs. Bacitracin use in the BC sentinel broiler and turkey flocks increased 95% and 242% in 2019 respectively, while none was used in the sentinel pig herds. This suggests the poultry industry's elimination of the preventive use of category II products might have been compensated for through increased use of bacitracin.

The poultry industry's Step 2 AMU strategy resulted in an 88% decrease of category II use in BC feed from 2017 levels which is a 25% reduction in use of medically important antibiotics in BC feed. The cessation of non-growth promotant use of penicillin accounted for 61% of the category II decrease and the reduced non-growth promotant use of virginiamycin accounted for 27% of the decrease.

The poultry industry's voluntary category II reduction combined with the 6.8% decrease of category II use from 2017 due to the growth promotion ban, accounts for the almost 95% decrease in category II use compared to 2017 use. As noted in the discussion of Figure 5, the growth promotion ban also resulted in 8.2% decrease in category III antibiotics from 2017 levels, although total use of category III antibiotics increased 36% from 2017 to 2021, and this largely offset the decreased use of category II antibiotics in BC feed.

In the BC in-feed antibiotic use data there was no detection of a change in AMU due to the federal regulatory change to require a prescription for use of all medically important animal antibiotics (except for the nitrofurans). This despite the vast majority of in-feed antibiotics for Canadian livestock and poultry were available without a prescription prior to 2018. A 2015 Evaluation of a Prescription Use Only Policy for Veterinary Antimicrobials report prepared for the Canadian Council of Chief Veterinary Officers found no evidence that such a policy in isolation would improve antimicrobial stewardship and reduce antimicrobial resistance[30].

The prescription requirement for almost all the products with medically important antibiotics virtually eliminated sale of non-feed antibiotics by licensees of BC's Veterinary Drug legislation because sales were restricted to veterinarians and pharmacists. As the latter two are not required to report their AMU information, this resulted in the loss of provincial AMU information and the associated reporting on AMU of these non-feed products.

The final 2018 federal AMU regulatory change was mandatory reporting of antibiotic sales by manufacturers, importers and compounders of antibiotics for animals. This included reporting by animal species and province or territory. As shown by CIPARS and BC Ministry of Agriculture AMU reports, more detailed AMU data at the animal species and geographical level are necessary to evaluate AMU. The stated purpose of the federal mandatory Veterinary Antimicrobial Sales Reporting (VASR) system is to support surveillance and analysis of the data, all of which was to be made publically available[10]. Yet to date, VASR has reported only very aggregated AMU data. For example, it has reported total antibiotic use by province, and this is not broken down by specific antibiotics or animal species. VASR reports total AMU by species but for the whole country, not by province and doesn't show the specific antibiotics used. It has reported AMU by antibiotic but for all animal species and all provinces combined. Prior to the mandatory federal reporting, the Canadian manufacturers of animal health products voluntarily provided annual antibiotic sales by province, and by antibiotic aggregated into two classes of animals: production animals and companion animals. Production animals included livestock, poultry and aquaculture, companion animals included dogs, cats and horses. The loss of detailed antibiotic reporting by drug, province and animal species is an unintended and unexpected consequence of the 2018 federal animal AMU regulatory changes.

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Appendix - Tables

Table 1. Annual Antibiotic Use In-feed Categorized by Importance in Human Medicine (gm active ingredient/tonne biomass)

	2002	2003	2004	2005	2006*	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Category I	- **	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Category II	20	12	7	7	7	8	6	13	24	12	14	16	15	16	15	19	14	1	1	1
Category III	59	51	47	66	37	72	82	82	52	57	70	51	55	53	52	49	50	60	64	67
Category IV	65	68	62	75	67	93	78	74	71	82	76	73	54	58	83	88	72	80	64	71
Not Categorized[a]	-	-	-	-	-	-	-	-	-	-	-	-	2	1	1	2	2	3	2	2
Total	145	131	117	148	111	172	166	169	147	151	160	141	126	127	151	158	139	144	130	141

* missing data

** no usage

[a] avilamycin

Table 2. Annual Antibiotic Use In-feed of Category IV Importance in Human Medicine (gm active ingredient/tonne biomass)

Antibiotic	2002	2003	2004	2005	2006*	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Bambermycin	0.08	0.08	0.07	0.13	0.13	0.06	0.01	0.02	0.01	0.01	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.18	0.07
Lasalocid	1.75	0.90	11.23	0.44	0.77	0.67	1.05	0.52	0.66	0.36	0.46	11.12	0.79	1.09	5.80	6.55	7.24	8.35	7.24	5.79
Salinomycin	16.77	18.07	13.64	16.66	9.86	24.69	23.79	20.68	1.58	8.29	10.52	14.63	11.02	18.14	23.91	25.98	10.98	16.37	18.87	23.10
Narasin	18.22	14.72	13.91	20.35	19.23	22.41	18.98	15.98	25.35	24.67	26.66	5.76	5.79	10.31	10.20	10.89	14.75	14.70	11.66	7.45
Monensin	28.30	34.32	23.18	37.64	37.32	44.81	34.15	36.57	42.92	48.73	38.32	41.87	36.75	28.08	42.91	44.32	39.38	40.61	26.06	34.91
Total	65.12	68.09	62.03	75.21	67.30	92.65	77.98	73.77	70.53	82.06	75.95	73.38	54.35	57.63	82.83	87.75	72.34	80.04	64.02	71.31

* missing data

Table 3. Annual Antibiotic Use In-feed of Category III Importance in Human Medicine (gm active ingredient/tonne biomass)

Antibiotic	2002	2003	2004	2005	2006*	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Bacitracin	26.44	21.50	26.29	52.11	29.60	53.60	60.98	56.86	30.60	41.62	47.96	32.39	33.63	34.17	36.98	33.23	34.95	55.50	57.85	55.23
Tetracyclines	29.20	26.35	18.18	11.64	6.62	16.08	18.24	21.37	17.36	13.15	17.33	14.99	17.39	14.43	12.01	13.28	13.40	4.81	5.86	11.36
Spectinomycin	0.26	0.27	0.28	0.29	0.22	0.16	0.19	0.18	0.09	0.07	0.03	0.04	0.03	0.01	0.01	0.04	- **	-	-	-
Sulfamethazine	3.54	2.79	2.71	1.61	0.13	1.80	2.32	3.30	4.04	1.99	4.03	3.55	3.29	3.72	2.72	2.01	1.64	-	-	-
Tiamulin	0.03	0.00	0.00	0.00	-	-	0.03	0.10	0.07	0.20	0.25	0.16	0.29	0.28	0.29	0.42	0.01	0.04	0.02	0.02
Total	59.47	50.92	47.46	65.65	36.56	71.64	81.76	81.81	52.15	57.02	69.61	51.12	54.64	52.61	52.00	48.97	49.99	60.35	63.73	66.62

* missing data

** no usage

Table 4. Annual Antibiotic Use In-feed of Category II Importance in Human Medicine (gm active ingredient/tonne biomass)

Antibiotic	2002	2003	2004	2005	2006*	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Erythromycin	- **	-	0.01	-	-	0.01	0.01	0.13	0.20	-	0.16	0.16	0.12	0.20	-	0.01	-	-	-	-
Lincomycin	0.72	0.84	0.65	0.80	1.17	0.77	0.49	0.18	0.09	0.07	0.08	0.12	0.10	0.02	0.01	0.04	-	-	-	-
Neomycin	0.34	1.35	0.86	0.04	0.22	-	-	-	-	0.09	-	-	-	-	-	-	-	-	-	-
Penicillin G	11.55	3.85	2.03	3.41	1.79	1.69	0.22	2.24	4.81	5.62	6.09	10.37	10.43	10.59	8.77	13.13	12.41	-	-	-
Tylosin	1.77	1.90	1.37	1.55	1.39	1.37	0.27	2.69	6.95	0.94	1.31	1.18	0.88	1.09	1.43	0.91	0.29	0.62	0.60	1.05
Virginiamycin	5.68	4.16	2.55	0.98	2.53	3.70	4.87	8.26	11.81	5.22	6.66	4.54	3.96	3.88	5.19	5.30	1.72	-	0.13	-
Total	20.06	12.10	7.47	6.79	7.10	7.54	5.85	13.50	23.86	11.93	14.30	16.37	15.49	15.78	15.40	19.38	14.43	0.62	0.73	1.05

* missing data

** no usage