Ottawa, September 12, 2025

Emailed to vdd.HSD-DIH.dmv@hc-sc.gc.ca

Health Canada
Veterinary Drug Directorate

Consultation: Categorization of antimicrobial drugs based on importance in human medicine

The Canadian Cattle Association (CCA) and the National Cattle Feeders' Association (NCFA) represent over 60,000 beef producers across the country. We work closely with veterinarians, livestock producers, and other stakeholders to promote responsible animal health practices. Beef producers' commitment to antimicrobial stewardship (AMS) is longstanding and well-documented, including significant investments in research and active participation in national initiatives like the Pan-Canadian Action Plan on Antimicrobial Resistance and the Animal Health Canada AMR Leadership Group.

CCA welcomes the opportunity to comment on Health Canada's proposed update to the **Categorization of Antimicrobial Drugs based on Importance in Human Medicine**. We support the need to update this scheme and believe that a credible national framework tailored to Canada's context is a valuable tool. We acknowledge that the 2023 Auditor General's Report on Antimicrobial Resistance recommended Health Canada to "update, as needed, its categorization of medically important antimicrobials to inform its priority setting so that stakeholders have the most current information to support the development of veterinary education programs and inform decisions about antimicrobial use." Unfortunately, we believe that the proposed recategorization misses the intended point by increasing the misalignment with the WHO and making it even harder for veterinarians and industry to make prudent use guidelines.

Health Canada identifies the major purposes of the categorization as (1) facilitating the regulation of veterinary antimicrobials and (2) providing the list of Medically Important Antimicrobials in conjunction with Health Canada's List A, to reduce the risk of antimicrobial resistance from their use in animals. Additional important uses include the guiding veterinary antimicrobial stewardship and classifying reported veterinary antimicrobial sales data[1] . We are concerned that the proposed changes will negatively affect all these applications.

Our concerns stem from the lack of transparency in the process leading to the proposed recategorization, the decision-making criteria used, and the stripping of Category III of any medically relevant drugs for veterinary medicine. Collectively, these concerns reflect a failure to apply a systems-based, One Health approach to this important tool. To address these issues, and to ensure Health Canada's categorization remains robust and credible for veterinary antimicrobial use policies, programs and prescriptions we call for three actions:

IMMEDIATELY PAUSE the proposed recategorization process and establish a credible One Health Committee that includes stakeholders external to Health Canada, with representation from livestock veterinarians and academia**.**

REVIEW the decision framework for antimicrobial categorization to ensure it is transparent, science-based, replicable, and considers the potential impact on antimicrobial stewardship in livestock.

CONDUCT A FORMAL RISK ASSESSMENT for antimicrobials that are proposed to transition from Category III (medium) to II (high), and that considers the relevant differences between different generations of drugs in the same category.

One Health Integration

The consultation documents do not specify which experts or stakeholders contributed to the proposed recategorization, creating uncertainty about the process. Given the complex and varied uses for the categorization scheme, this work should be guided by a multidisciplinary advisory committee to ensure all One Health perspectives are represented. For example, the World Health Organization established an Advisory Group on Critically Important Antimicrobials for Human Medicine and commissioned a technical group that included 17 experts from human, veterinary, agriculture and environmental sectors. This approach ensured the perspectives of diverse disciplines were accounted for. A similar process is required for Canada's categorization to remain credible and avoid the unintended consequences we are concerned about.

Categorization Methodology and Decision Criteria

The Health Canada consultation recognizes that AMR is a One Health issue yet continues to frame the scheme from a human-centric approach. The core criteria remain based on (1) indications for human use in serious or life-threatening infections and (2) the availability of alternatives to treat humans. In contrast, the WHO categorization considers whether an antimicrobial is the sole/limited therapy for serious human infections as well as the risk of resistance transmission from non-human use.

Health Canada's criteria and evaluation methods appear to be consistent with the 2009 publication. However, since then Canada has generated a significant body of evidence on the links between animal AMU and human AMR through surveillance and research. Canada has data on the trends in antimicrobial use in food animals and corresponding trends in resistance patterns. The Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) and FoodNet Canada have been monitoring AMR for decades and provides valuable information on the contribution of farm-level AMU to AMR in both animal and human derived bacteria. This information is complementary to the many peer-reviewed publications generated in Canada on this topic. Admittedly, the scientific community's understanding of the causal association pathways remains incomplete, but this classification should reflect the current state of our collective scientific knowledge. Exclusively considering human antimicrobial needs risks negative effects on animal health and welfare without providing benefit to human health.

The Health Canada categorization stratifies only to the drug class level, with little separation of subgroups or separate classifications for various products within a class. This differs from the more granular approach taken by the WHO which separates out specific drugs within classes where stewardship stakes are different. Categorizing at the class level rather than distinguishing subclasses or drugs results in some drugs that are used either solely (e.g., florfenicol) or almost exclusively in livestock (e.g., first generation tetracyclines) being categorized as "high importance." This lack of granularity limits the usefulness of the categorization for veterinary stewardship guidance.

Health Canada uses a risk-assessment framework for most major decisions. We propose that the expert committee be tasked with reviewing the methodology and decision criteria. A risk-based approach should consider evidence of resistance transmission, the extent of antimicrobial use in humans, and the requirements for antimicrobial use in livestock. This approach would allow the categorization to continue to inform stewardship guidelines and ensure the methods are transparent and replicable for future reviews.

Assessment of proposed recategorization and stewardship implications

The CCA and NCFA support the antimicrobial drug classes proposed for Category I and Category IV. We agree with placing critical antimicrobials in Category I, as these drugs are vital for the protection of the health of Canadians. We also applaud the decision to retain Category IV, which designates antimicrobial classes not used in human medicine as not-medically important. Retaining Category IV preserves the ability to use ionophores as an antimicrobial-sparing tool to support cattle health.

However, the proposal appears to undervalue the categorization system's role as a cornerstone of stewardship messaging across the livestock industry. For example, Category I drugs are used sparingly, representing less than 1% of total use, and are subject to strict regulations[1]. Their use is limited to fluoroquinolones and third-generation cephalosporins. These are the only Category I antimicrobials licenced for use in food animals in Canada. These products have restrictive label claims that preclude prophylactic use. In addition, industry stewardship guidelines, Veterinary Prudent Use Guidelines, and decision-support tools emphasize that these drugs should be reserved as "last-resort" choices when no effective alternatives exist. Together, these safeguards show how the categorization scheme can be leveraged for education, awareness, and stewardship.

The proposed recategorization strips Category III of practically all useful antimicrobials for veterinary medicine. In essence, the new proposal leaves Canadian veterinarians with a simplified three-tier system for prescribing decisions. This direction is opposite to the 2024 WHO prioritization scheme which now has six categories, five of which include antimicrobials authorized for non-human use.

Maintaining a distinction between Category II and III is crucial. Stewardship efforts are guided by the principle of "as much as necessary, as little as possible," and within that framework, refinement in drug class selection is key. Stewardship guidelines encourage veterinarians to start with the lowest category drug that is expected to be effective. Reclassifying older, commonly used drugs from Category III to II, including the aminoglycosides, phenicols, pleuromutilins, and all tetracyclines, will erode incentives to preserve the current Category II drugs.

The proposed movement of many drug classes from Category III to Category II will distort antimicrobial use reporting. All surveillance and benchmarking programs rely upon consistent reporting. The benefit of a methodology change must outweigh the cost of distorting long-term trend analysis. Canada reports veterinary antimicrobial sales data by antimicrobial class. This reporting has demonstrated progress in responsible use over the last decade. In 2023, Category III drugs accounted for 68% of use, compared to 29% for Category II [1]. This is a significant shift from 2015, when the split was nearly even between the two categories. This change demonstrates active stewardship initiatives on the part of livestock veterinarians and producers. If the proposed categorization is accepted, the expanded scope of Category II will result in an artificial increase in the reported use of high-importance antimicrobials even in the absence of any prescribing change. Conversely, if pressures rise for AMU reduction, prescribers may shift from current Category III products such as chlortetracycline to current category II drugs such as virginiamycin which have lower label dosages to simply appear to be using a lower quantity of antimicrobials, counter to current stewardship messaging.

Case example: recategorization of first and second generation tetracyclines

Health Canada is proposing recategorizing first and second generation tetracyclines from Category III to Category II. This proposed change will have meaningful impact on beef cattle production, and we use this proposed recategorization to provide a case example of the systemic process concerns raised in our response.

We appreciate Health Canada sharing their rationale and justification for the proposed categorization. In 2023, tetracyclines were the 9th most common antimicrobial class used in Canadians (people) and the most common class used in livestock[2].

Indications for tetracycline use in people are provided by Health Canada. Among those listed under 'tetracyclines (not generation specific)' two pathogens are Tier 1 (High Priority) on Health Canada's Priority Pathogen List.

Drug resistant *Neisseria gonorrhoeae* is a Tier 1 pathogen. Tetracycline resistance in gonorrhea is primarily mediated by a point mutation [3]. AMR from use of tetracycline in livestock is implied to be from transferrable elements. This suggests there is not a clear pathway for tetracycline use in livestock to contribute to meaningful clinical resistance in tetracycline resistance in human gonorrhea infections.

Carbapenem resistant *Acinetobacter* spp is also listed as a Tier I Priority pathogen for which tetracycline is indicated. The Infectious Diseases Society of America guidelines for treatment of Carbapenem Resistant *Acinetobacter* [4] indicates that a newer generation tetracycline such as minocycline or tigecycline could provide the third agent in a high-dose combination therapy along with ampicillin and sulbactam. The guidelines do not recommend first or second generation

[1] 2023 Veterinary Antimicrobial Sales Highlights Report - Canada.ca
[2] CIPARS 2023 report
[3] https://pmc.ncbi.nlm.nih.gov/articles/PMC1251527/
[4] IDSA 2024 Guidance on the Treatment of Antimicrobial Resistant Gram-Negative Infections

tetracyclines. The resistance mechanisms for third to fifth generation tetracyclines differ from first and second generation tetracyclines[5].

Preserving therapeutic options for serious human infections is of the utmost importance to all stakeholders committed to addressing AMR. However, we call for the need a nuanced consideration of clinical situations where the use of older tetracyclines in people remains important. Health Canada notes that "As *tet* resistance determinants may coexist with other resistance genes in gene clusters or resistance gene cassettes, co-selection of resistance is an issue of concern." Clarification about the relative weighting of co-selection is required given this is not one of the major stated criteria for classification.

In Canada, only first generation tetracyclines are used in livestock. Tetracycline use includes chlortetracycline and oxytetracycline. These are the most used antimicrobial class in beef cattle, dairy cattle, and pigs. In beef cattle, the primary indication for use is the prevention, control and treatment of liver abscesses. This use is critical to protecting animal health and welfare. There is a high prevalence of resistance to first generation tetracyclines in many other veterinary pathogens but, despite this, the product remains highly effective for addressing liver abscesses.

Recategorizing first generation tetracyclines as Category II would result in all antimicrobial drugs appropriate for liver abscess therapy being Category II. The other antimicrobials used for this purpose are tylosin and virginiamycin. Macrolides are the mainstay drug class for Bovine Respiratory Disease (BRD). BRD is the beef sector's most pressing infectious animal health issue. AMRNet reports that two of the common bacterial pathogens in BRD, *Manheimia haemolytica* and *Pasturella multocida,* have the highest rate of resistance to tetracycline while resistance rates to macrolides are lower.

Recategorizing first generation tetracyclines to share could lead to a shift in use from tetracycline to macrolides, that could result in a potential increase in resistance in BRD pathogens (CIPARS 2024 Stakeholder Webinar Integrated deck EN_FINAL.pdf). We feel this possibility is of sufficient probability and consequence that the proposed recategorization of first generation tetracyclines as high importance deserves careful reconsideration.

This tetracycline case example was developed based on consultation with experts involved in many aspects of veterinary medicine and One Health. It includes the perspectives of producers, practicing veterinarians, researchers in beef cattle health, epidemiology, pharmacology and public health as well as federal and provincial veterinarians involved in surveillance and animal health regulation. We admit our perspective lacks input from medical doctors and human-centric research and would welcome the opportunity to expand our understanding of the One Health perspective on this important topic. We believe that if we, as veterinary and animal health stakeholders, struggle to fully understand the rationale behind certain recategorization decisions, it is likely that those from the medical and public health community may also find it difficult to appreciate the animal health and production implications. **This lack of shared understanding is precisely why we believe a formal One Health committee would be so valuable.**

[5] https://doi.org/10.1038/s41467-025-56425-5

Moving forward

The **Stewardship pillar** of the **Pan-Canadian Action Plan on Antimicrobial Resistance (AMR)** outlines a **collaborative approach** between the **federal government and industry**, aiming to promote responsible antimicrobial use and reduce resistance across human, animal, and environmental sectors. For this reason, we encourage the federal government to continue working with us in a collaborative way, rather than moving forward with changes on its own. Decisions on drug categorization or policies are most effective when developed together, as unilateral changes can unintentionally create challenges for animal health, trade, and Canada's overall stewardship goals.

The lack of transparency, readily available methodology, and decision-making criteria underpinning the current recategorization completely devalues the utility and validity of the categorization system. We urge Health Canada to consider the implementation of our recommendations to support stewardship messaging, reporting and surveillance objectives, and animal health and welfare, while preserving effectiveness for all who may rely on antimicrobial therapy.

Only through a balanced, evidence-based approach can we ensure the continued effectiveness of Canada's antimicrobial stewardship efforts. We appreciate the opportunity to comment on the Proposed Categorization of Antimicrobial Drugs Based on Importance to Human Medicine (Third Version – June 2025 – Draft for Public Consultation) and welcome continued engagement with the Veterinary Drugs Directorate on this important initiative.

Sincerely,

Dr. Leigh Rosengren
Chief Veterinary Officer
Canadian Cattle Association

Melissa Downing
Director, Regulatory and Sustainability
National Cattle Feeders' Association