Review Article Compte rendu

Review of antimicrobial therapy of selected bacterial diseases in broiler chickens in Canada

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Abstract — This paper reviews common therapeutic applications of antimicrobials in broiler chicken production in relation to Canadian guidelines, surveillance data, and emerging public health concerns about antimicrobial use (AMU). *Escherichia coli, Clostridium perfringens,* and *Staphylococcus* spp., were reviewed because of their animal health and economic significance. *Enterococcus cecorum* and *Salmonella* were included because of their importance in antimicrobial resistance (AMR) surveillance. This review identified that i) antimicrobials are available in Canada to treat infections by these agents, but may be through over the counter or extra-label use, ii) prevalence rates for these diseases are unknown, iii) antimicrobial use estimates in broilers are lacking, and iv) AMR has emerged in clinical isolates, though data are very sparse. This review highlights the need for surveillance of AMU and AMR in broiler chickens in Canada.

Résumé — Revue des thérapies antimicrobiennes pour certaines maladies bactériennes chez les poulets à griller au Canada. Le présent article passe en revue les applications thérapeutiques courantes d'antimicrobiens au sein de la population de poulets à griller en rapport avec les lignes directrices canadiennes, les données de surveillance et les préoccupations nouvelles de santé publique à propos de l'usage des antimicrobiens. *Escherichia coli, Clostridium perfringens* et *Staphylococcus* spp. ont été examinés en raison de leur importance pour la santé animale et la situation financière. *Enterococcus cecorum* et *Salmonella* ont été inclus en raison de leur importance pour la surveillance de la résistance aux antimicrobiens. Cette revue a identifié que i) des antimicrobiens sont disponibles au Canada pour traiter des infections par ces agents, mais peut-être avec l'utilisation de produits en vente libre ou en dérogation des directives de l'étiquette, ii) les taux de prévalence de ces maladies sont inconnus, iii) il y a une absence d'estimations pour l'utilisation des antimicrobiens et iv) la résistance aux antimicrobiens s'est présentée dans des isolats cliniques, quoique les données soient très rares. Cette étude souligne le besoin de surveillance de l'utilisation des antimicrobiens et de la résistance aux antimicrobiens chez les poulets à griller au Canada.

(Traduit par Isabelle Vallières)

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Introduction

Surveillance systems in Canada and the United States have highlighted the importance of poultry as a source of foodborne diseases and antimicrobial-resistant organisms (1–3). Food safety and biosecurity programs have been implemented to address these foodborne hazards and infectious diseases. Veterinarians and producers may use antimicrobials for growth promotion, disease prophylaxis, and treatment in compliance with industry food safety programs (4). Prudent use guidelines are also available to veterinarians (5).

In Canada, bacterial diseases of broilers are not routinely monitored or reported. In the absence of information regarding the prevalence of broiler diseases, the bacterial pathogens *Escherichia coli, Clostridium perfringens,* and *Staphylococcus* spp. were reviewed because of their persistence in broiler poultry. These were also included in the Canadian Veterinary Medical Association's–Prudent Use Guidelines (CVMA-pug) (5). *Enterococcus cecorum,* an emerging pathogen of Canadian broilers (6), and *Salmonella* (2), a zoonotic pathogen, are also included.

This review provides a comprehensive picture of common therapeutic AMU in Canadian broilers with the intent to inform prudent use guidelines for veterinarians and producers and to identify elements for national surveillance programs.

Materials and methods

Information regarding the availability of antimicrobials for use in broiler chickens to treat infections due to *E. coli,*

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C. perfringens, Staphylococcus spp., *E. cecorum,* and *Salmonella* in Canada was gathered from the Compendium of Veterinary Products (CVP) (7), the Compendium of Medicating Ingredient Brochure (CMIB) (8), and the CVMA-pug (5). These documents provide information on indications, dosage, duration, and route of administration under Canadian conditions. Antimicrobials were grouped according to their importance to human medicine, using the categorization system of Health Canada's Veterinary Drugs Directorate (VDD) as follows: Category I — Very High Importance; Category II — High Importance; Category III — Medium Importance, and Category IV — Low Importance (9). Use of VDD's categories enables a better understanding of current broiler AMU practices in light of their potential public health impact in Canada. The World Health Organization (WHO) drug categorization system was also consulted (10). Conditions for use and marketing status for each drug were summarized. A comprehensive report pertaining to AMU regulations in Canada was also consulted (11).

For efficacy data, peer-reviewed literature searches of PubMed, Scopus, and Agricola databases, and online poultry journal sources were conducted using the following search string: "*Escherichia coli* (or *Staphylococci* or *Clostridium perfringens* or *Salmonella* or *Enterococcus cecorum*) and chickens (or broilers or poultry or avian) and antimicrobial (or antibiotics or therapy or prevention or control) and ceftiofur (or any of the specific antimicrobials)." Non-Canadian studies were also assessed, since there were few Canadian studies. Additional references were consulted including pharmacokinetic studies, and safety and toxicity studies in the absence of efficacy studies.

Published data of passive surveillance (1,12), laboratory reports (13,14) and Canadian peer-reviewed publications (15,16) were consulted to determine AMR profiles of clinical isolates.

Results and discussion

Stewardship of antimicrobial use in the Canadian poultry industry

The prudent use of antimicrobials in food animals is a collaborative effort involving veterinarians, industry/commodity groups, and government to preserve antimicrobial efficacy, and to reduce the risk of AMR-microorganisms or antimicrobial residues entering the food chain. Prudent use practices should prioritize the preservation of antimicrobials considered to be important to human medicine [VDD's classification system (9)]. Similar to VDD's classification system, the WHO categorized antimicrobials as either critically important, highly important, or important (10). The VDD's Category I and some of VDD's Categories II and III drugs are considered critically important by the WHO because of the importance of these drugs for the treatment of human illnesses in other areas of the globe.

Approved veterinary antimicrobials in Canada are listed in the CVP (7). Table 1 lists antimicrobials cited by various researchers worldwide for therapy of the selected bacterial diseases; however, some of these antimicrobials would have to be used in an extra-label manner in Canada because they are not approved for 1 or more of the following: i) use in chickens, ii) indications (e.g., target pathogens and/or disease conditions), iii) route of administration, and/or iv) dosage. The VDD has developed an extra-label drug use (ELDU) policy to minimize risks of this practice to consumers, animals, and the environment (17). In the CVMA-pug (5) there are also drugs suggested for use in broilers that would have to be administered in an extra-label manner, also referred to as "off-label use." Some of the antimicrobials cited require a veterinary prescription (7). For the manufacture of medicated broiler feeds, feedmills comply with the CMIB (8) and veterinary prescriptions are needed for the inclusion of antimicrobials that are ELDU in-feed (4). Feed manufacturing, including labelling, is monitored by the Canadian Food Inspection Agency (CFIA) under the *Feeds Act* and *Health of Animals Act* (18). Table 2 summarizes all drugs listed in the CVMA-pug and CMIB for use in broilers.

Drugs for veterinary use are approved for sale by the VDD, whereas the dispensing of drugs (i.e., once approved at the federal level), prescription and over-the-counter (OTC) sales, are regulated at the provincial level (11). Prudent use (e.g., the CVMA-pug, fact sheets on AMU/AMR, CFIA Meat Inspection Procedures) and food safety guidelines (e.g., Chicken Farmer of Canada's *Safe, Safer, Safest* program), and provincial legislation (e.g., Ontario's *Livestock Medicines Act, Alberta Livestock Disease Act,* and *Veterinary Profession Act*) encourage veterinarians and producers to use antimicrobials in the context of a valid veterinarian-client-patient relationship (4,5,19). However, gaps still exist in AMU knowledge such as own use importation (OUI) and use/compounding of imported active pharmaceutical ingredients (API), which are unregulated practices in Canada (11). Broiler-specific AMU information is unavailable (1) and the extent of OTC purchases versus veterinary-prescribed purchases for breeder, hatchery, or broiler farm use in Canada is also unknown.

A growing global concern with AMR has resulted in the implementation of programs for monitoring antimicrobial use and resistance (AMU/R) in food animals and humans. The Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) (1) is a national AMU/R program which targets selected indicator and zoonotic organisms from humans, animals, and animal-derived sources. A national farm surveillance of AMU/R in broilers will be implemented by CIPARS in collaboration with the poultry industry in 2012 to gather broiler AMU estimates. Surveillance of important pathogens, though recommended by a 2002 advisory committee to Health Canada (11), is not covered by CIPARS or any surveillance program in Canada.

Antimicrobial therapy of selected broiler diseases

Escherichia coli infections

Colibacillosis is one of the most important diseases affecting broiler chickens worldwide and encompasses a wide range of localized and systemic diseases in broiler chickens and other avian species (20). Some avian pathogenic *E. coli* (APEC) strains may be zoonotic (21,22). The current prevalence rate of colibacillosis in broilers is unknown.

Therapeutic options, grouped into first, second, and last choices (23), are not yet established in Canada. Typical

Table 1. Availability of antimicrobials for use in chickens in Canada

	Antimicrobials available	Microorganism and/or disease for which antimicrobial is approved	Animal species for which anti-microbial is approved	Routes of administration and dosage in approved animal species	Comments/cautions/ warnings by manufacturer
I[a]	Ceftiofur *(Excenel)*[b]	Various Gram +/−, *Salmonella* *E. coli*	Cattle, pigs, horses, dogs, lambs, turkeys	SC: 0.17 mg/poult as a single injection	Rx[c] ELDU[d] if administered SC/*in-ovo* in chicks *"The ELDU of Excenel is not recommended"*
	Enrofloxacin *(Baytril)*	*Mannheimia haemolytica,* *Pasteurella multocida* Various Gram +/−	Beef cattle dogs cats	SC: 7.5–12.5 mg/kg PO: 5–20 mg/kg IM: 2.5 mg/kg PO: 5 mg/kg	Rx ELDU for use in chickens, any route *"Do not use in an ELDU manner in cattle or in any other species"*
II	Ampicillin *(Polyflex)*	Various Gram +/−	Dogs, cats, cattle, pigs	SC/IM: 6–6.5 mg/kg	ELDU if used in chickens
	Amoxicillin *(Paracillin)*	*E. coli* *Salmonella*	Chickens, pigs	PO: 8–16 mg/kg	Rx ELDU if used for *C. perfringens* and *Staphylococcus* spp.
	Apramycin *(Apralan)*	*E. coli*	Pigs	PO (water): 12.5 mg/kg	ELDU if used in chickens
	Gentamicin *(Gentocin)*	*E. coli* *Salmonella* Typhimurium *Pseudomonas aeruginosa*	Chickens	SC: 0.2 mg/chick as a single injection	Rx ELDU if administered *in-ovo*
	Lincomycin-Spectinomycin *(Linco-Spectin)*	*Staphylococcus* *Pasteurella multocida* *Streptococcus* spp. *Mycoplasma* spp.	Dogs, cats	IM: 20 mg/kg	ELDU if administered SC/*in-ovo* in chicks *"For intramuscular use in dogs and cats only"*
	Lincomycin (L)-Spectinomycin (S) *(LS 20 Premix)*	Swine dysentery	Pigs	PO (feed): 22 mg/kg L, 22 mg/kg S	ELDU if used in chickens
	Ormethoprim-sulfadimethoxine *(Romet)*	*Aeromonas salmonicida*	Salmon/trout	PO (feed):15 mg/kg	Rx ELDU if used in chickens
	Penicillin G Potassium *(Pot-Pen)*	*Clostridium perfringens*	Chickens	PO (water): 297 000 IU/L	ELDU if used to treat other pathogens in chickens
	Penicillin G Potassium *(USP Soluble powder)*	*Erysipelothrix rhusiopathiae*	Turkeys	PO (water): 297 000 IU/L	ELDU if used to treat other pathogens in chickens
	Trimethoprim-sulfadiazine *(Tribrissen)*	*Vibrio angularium*	Salmon	PO (feed): 30 mg/kg	Rx ELDU if used in chickens
		Various Gram +/−	Dogs, cats cats	SC:30 mg/kg	Rx ELDU if used in chickens
	Virginiamycin *(Stafac)*	Necrotic enteritis (prevention only)	Broilers	PO (feed): 22 mg/kg	ELDU if used at higher dosage
III	Bacitracin *(Albac, BMD)*	Necrotic enteritis (prevention only)	Broilers	PO (feed): 55 mg/kg	ELDU if used at higher dosage
	Spectinomycin *(Spectam)*	*Pasteurella multocida*	Turkeys	SC: 11–22 mg/kg	ELDU if administered SC/*in-ovo* use in chickens
	Sulfamethazine *(Sulfa-"25")*	Coccidiosis	Chickens	PO (water): 35 mL/9 L	ELDU if used to treat *E. coli* in chickens
	Sulfaquinoxaline *(Sulfaquinoxaline 19.2% Liq conc.)*	Coccidiosis *Pasteurella multocida* *Salmonella* Pullorum, *S.* Gallinarum	Chickens	PO (water): 90 mL/45.4 L	ELDU if used to treat *E. coli* in chickens

SC — subcutaneous; PO — *per os* (by mouth), im — intramuscular.
[a] Roman numerals I to III indicate the ranking of antimicrobials based on importance in human medicine as outlined by the Veterinary Drugs Directorate, Health Canada (9).
[b] Compendium of Veterinary Products (7) and CMIB (8); some information may have been updated at the time of writing.
[c] Rx — Prescription only.
[d] ELDU — Extra-Label Drug Use.

Table 2. Antimicrobials included in Canadian guidelines for use in broiler chickens

Disease	Antimicrobials included in the CVMA-pug[a]	Antimicrobials (for use in-feed) included in the CMIB[b]
E. coli — omphalitis	Gentamicin (SC route only), *lincomycin-spectinomycin*	
E. coli — airsacculitis	Amoxicillin, *ormethoprim-sulfadimethoxine, trimethoprim-sulfadiazine, sulfamethazine, sulfaquinoxaline,* tetracycline, tetracycline-neomycin	Chronic respiratory disease: Chlortetracycline, erythromycin, oxytetracycline
E. coli — arthritis	Amoxicillin, *ormethoprim-sulfadimethoxine,* oxytetracycline, tetracycline, *trimethoprim-sulfadiazine*	
C. perfringens — necrotic enteritis	Bacitracin, lincomycin, neomycin, penicillin, tetracycline, *trimethoprim-sulfadiazine,* tylosin,	Necrotic enteritis: Bacitracin, virginiamycin, narasin, tylosin
Staphylococcus — arthritis	Erythromycin, *ormethoprim-sulfadimethoxine, penicillin,* tetracycline	
Non-specific enteritis		Chlortetracycline, oxytetracycline

[a] Canadian Veterinary Medical Association — Prudent Use Guidelines. Italicized antimicrobials are extra-label drug use (ELDU) for species, dose, or indications (5).
[b] Compendium of Medicating Ingredient Brochure (8).

first choice drugs for colibacillosis include potentiated sulfas (e.g., ormethoprim-sulfadimethoxine, trimethoprim-sulfadiazine). Second choice drugs are the aminopenicillins (e.g., ampicillin, amoxicillin), tetracyclines (e.g., chlortetracycline and oxytetracycline), colistin, and the aminoglycosides (e.g., neomycin, gentamicin, and spectinomycin). The third or last choice drug is enrofloxacin, recommended for use only when all other options have failed (23). Table 3 summarizes data for 16 antimicrobials based on these choices, plus those included in other published references (24).

Information was obtained from peer-reviewed publications conducted worldwide from 1976 to 2011, investigating the clinical efficacy and/or pharmacokinetic parameters of these drugs. Broiler-type chicken strains were used as models for these studies with the exception of a study that used turkeys (25) and a study that used leghorn-type strains (26). Table 3 includes drugs belonging to the VDD's Categories I to III which are available in Canada for veterinary use; however, 10 of these would have to be used in an extra-label use manner. Two of the potentiated sulfa drugs cited [trimethoprim-sulfadimethoxine and trimethoprim-sulfaquinoxaline (27)] are unavailable in Canada. Neomycin, spectinomycin, and the tetracyclines can be purchased OTC and used following label instructions for *per os* (PO) administration. Amoxicillin, gentamicin, lincomycin-spectinomycin, ormethoprim-sulfadimethoxine, trimethoprim-sulfadiazine, sulfamethazine, and sulfaquinoxaline were included in the CVMA-pug list for therapy of *E. coli* conditions in broilers, plus other drugs such as tetracycline and tetracycline-neomycin, though there was no *in-vivo* or *in-vitro* data for this drug combination (Table 2). For in-feed medication, the CMIB included the tetracyclines for the therapy of chronic respiratory disease (CRD)/airsacculitis.

As described in Table 1, manufacturers recommended prescription-only medication and included warnings on the product labels for the VDD's Category I, and a few drugs belonging to Category II (amoxicillin and gentamicin), and III (florfenicol). The VDD ELDU policy states that Category I antimicrobials are not recommended for mass medication in an ELDU manner in Canada (17). In other countries, the use of antimicrobials important to human medicine is restricted. For example, in Denmark, fluoroquinolones can only be prescribed after conducting laboratory tests verifying that the target pathogen is not susceptible to any other approved antimicrobial (28). In the face of acute disease, treatment may be initiated pending laboratory results; however, if the pathogen is found to be susceptible to non-fluoroquinolone antimicrobials, then these drugs must be used. Similarly in the United States, the drug enrofloxacin is no longer permitted for use in chickens after the US Food and Drug Administration's (FDA's) decision to withdraw its approval in July 2005 based on a risk assessment of human consumption of chicken contaminated with fluoroquinolone-resistant *Campylobacter* spp. (29). In Canada, fluoroquinolone use in broilers is extra-label (Table 1). Ceftiofur, which falls within VDD's Category I, has an updated label with a warning "The extra-label drug use of EXCENEL Sterile Powder is not recommended" (5,7). The CVMA-pug also states: "in an outbreak situation, and for a short-term use, ceftiofur, a VDD category I antimicrobial, might be used" (5). Given the public health concern with the ELDU of ceftiofur (19), use of lower category drugs and management alternatives should be explored. Alternatives to reduce APEC and thus potentially AMU include strict grading of hatching eggs for setting, and effective cleaning of laying equipment/egg storage facilities and hatchery premises.

Escherichia coli can infect chickens throughout their lifespan (20); the most convenient and practical route of administration (mass medication) should be considered along with operational/industry factors (24,30). At the hatchery, antimicrobials are administered either in a subcutaneous (SC) or an *in-ovo* manner (24). The basis for hatchery use has not been fully established, and this is a life stage where there is the presence of other pathogens (e.g., environmental or vertically transmitted) (20) and chicks are highly susceptible to infection (31). Ceftiofur was investigated for the therapy of neonatal bacterial infections and was found to be efficacious (32). Available third generation cephalosporins are indicated for parenteral administration (7). In poultry, ceftiofur is routinely co-administered SC with Marek's Disease vaccine (33). In the US, ceftiofur was approved by the FDA as a single SC injection in day-of-age broiler chicks at the recommended rate of 0.08 to 0.20 mg/chick (34). *In-ovo* administration at day 18 of embryogenesis is an alternative to SC, but ceftiofur is not labelled for *in-ovo* applications in either

Table 3. Review of antimicrobials for treatment of *Escherichia coli* infections in chickens and turkeys

	Antimicrobial[a]	Type of study	*n*[b]	Duration and dose	Route	Comments	Year (Reference)
I[c]	Ceftiofur	*In-vivo*/dose-finding, broilers	—	Once: 0.08–0.20 mg/chick	SC	↓ mortality, ↓ lesions	1992 (32)
	Enrofloxacin	*In-vivo*/comparative efficacy, broilers	1600	3 d: 25 ppm (3.23% product)	PO (water)	↓ mortality, ↓ lesions	2004 (87)
		In-vivo/efficacy, leghorns	360	5 d: 10 mg/kg (10% product)	PO (water)	↓ mortality, ↓ lesions	2011 (26)
II	Amoxicillin	*In-vivo*/efficacy, leghorns	360	5 d: 10 mg/kg 5 days	PO (water)	mortality and lesions persisted	2011 (26)
	Ampicillin	*In-vivo*/efficacy and pharmacokinetics, broilers	—	4 d: 1.65 g/L	PO (water)	↓ mortality, ↓ lesions, optimum dose confirmed	1981 (39)
	Apramycin	*In-vivo*/efficacy, broilers	922	1 to 2 d: 0.5 g/L	PO (water)	↓ colonization	2001 (81)
	Gentamicin	*In-vivo*/efficacy, leghorns and broilers	12 000	Once: 0.2 mg/chick	SC	↓ mortality, ↑ production efficiency	1976 (82)
	Lincomycin (L)-Spectinomycin (Sp)	*In-vivo*/efficacy, broilers	2365	Once: 2.5 mg L, 5.0 mg Sp	SC	↓ mortality, ↓ bacterial recovery	1979 (37)
	Neomycin	*In-vivo*/efficacy, safety, and toxicity, turkeys	2880	5 d: 11–22 mg/kg	PO (water)	↓ mortality, no known toxic effect	2000 (25)
	Ormethoprim (O)-Sulfadimethoxine (Sm)	*In-vivo*/efficacy, broilers	201	24 d: 68.1 g O and 113.5 g Sm/lb of feed base	PO (feed)	Prophylactic and therapeutic activity confirmed	1979 (38)
	Trimethoprim (Tm)-Sulfadiazine (Sd)	*In-vivo*/efficacy, pharmacokinetic, broilers	~600	4 d: 66–330 mg/L Tm, 250 mg/L Sd	PO (water)	Ratio of 1:3 to 1:5 was optimal	1984 (83)
III	Chlortetracycline	*In-vivo*/efficacy, broiler breeder males	480	3 d: 4.5 g/L	PO (water)	↓ mortality, ↓ lesions	1977 (84)
	Florfenicol	*In-vivo*/pharmacokinetic in healthy/sick broilers	35	Once: 30 mg/kg	PO (water)	Confirmed dosage, twice daily was optimal	2002 (85)
	Oxytetracycline	*In-vivo*/efficacy in leghorns	360	3 d: 20 mg/kg	PO (water)	↓ mortality, ↓ lesions	2011 (26)
	Sulfadimethoxine	*In-vivo*/comparative efficacy, broilers	1600	6 d: 1875 mg/gal	PO (water)	Moderate ↓ in mortality/lesions	2004 (87)
	Spectinomycin	*In-vivo*/efficacy, broilers	~600	5 d: 51.1 mg/L	PO (water)	↓ lesions	1988 (86)
	Sulfaquinoxaline	*In-vivo*/pharmacokinetic, broilers	~600	4 d: 200 mg/L	PO (water)	Confirmed optimal dose	1984 (83)
		In-vivo/potentiation and synergistic mixtures, broilers	~176	7 d: 333 mg/L	PO (water)	Lesions persisted without Tm mixture	1983 (27)

SC — subcutaneous, PO — *per os* (by mouth)
[a] Cited by various authors and are available in Canada for veterinary use.
[b] Otherwise indicated, *n* refers to the total number of animals used in the study.
[c] Roman numerals I to III indicate the ranking of antimicrobials based on importance in human medicine as outlined by the Veterinary Drugs Directorate, Health Canada (9).

Canada or the US. More recently, the US FDA issued a docket (No. FDA-2008-N-0326) prohibiting certain extra-label uses of cephalosporins in food animals, including *in-ovo* applications (35). More data are required to determine the impact on early gut flora, efficacy, safety, and economics of ceftiofur use, particularly in light of emerging AMR observed in Canadian *E. coli* isolates from chicken and more importantly the strong correlation ($r = 0.9$, $P < 0.0001$) of ceftiofur resistance observed in chicken and human *Salmonella* Heidelberg isolates in the province of Québec (36).

Another antimicrobial approved for SC administration in broiler chicks in Canada is gentamicin. The 35-day withdrawal period required for gentamicin (7) limits its use in broilers because of their relatively short lifespan.

Lincomycin-spectinomycin (37), a VDD Category II drug, is listed in the CVMA-pug for treating *E. coli,* but this use would

Table 4. Summary of antimicrobial resistance in diagnostic submissions and passive surveillance of avian species across Canada

		Gram negatives				Gram positives			
		E. coli		*Salmonella*		*C. perfringens*		*S. aureus* and *S. hyicus*	
	Antimicrobial	Prevalence of resistance (MAPAQ)[a] *n* = 261	Resistant zones (mm), disc conc. (μg)[b]	Prevalence of resistance (CIPARS)[c] *n* = 209	Resistant MIC[d] (μg/mL)	Prevalence of resistance (AHL)[e] *n* = 100	Resistant MIC[f] (μg/mL)	Prevalence of resistance (MAPAQ)[a] *n* = 63	Resistant zones (mm), disc conc. (μg)[b]
I[g]	Ceftiofur	***43%***	≤ 17 (30)	16%	≥ 8	—	—	0%	≤ 17 (30)
	Ciprofloxacin	—	—	0%	≥ 4	—	—	—	—
	Enrofloxacin	6%	≤ 16 (5)	—	—	—	—	***11%***	≤ 16 (5)
II	Ampicillin	55%	≤ 13 (10)	21%	≥ 32	—	—	10%	≤ 28 (10)
	Erythromycin	—	—	—	—	2%	≥ 8	—	—
	Gentamicin	36%	≤ 12 (10)	2%	≥ 16	—	—	—	—
	Neomycin	***8%***	≤ 12 (30)	—	—	—	—	10%	≤ 12 (30)
	Penicillin	—	—	—	—	—	—	—	—
	Trimethoprim-sulfa	7%	≤ 10 (1.25/23.75)	0%	≥ 4/76	—	—	0%	≤ 10 (1.25/23.75)
	Virginiamycin	—	—	—	—	25%	≥ 2	—	—
III	Bacitracin	—	—	—	—	64%	≥ 16	—	—
	Florfenicol	—	—	—	—	0%	≥ 4	—	—
	Tetracycline	58%	≤ 14 (30)	18%	≥ 16	62%	≥ 2	22%	≤ 14 (30)

[a] MAPAQ — Ministère de l'Agriculture, des Pêcheries et de l'Alimentation du Québec, passive surveillance of avian isolates in Québec in 2010. Percentages in italicized and bold fonts for *E. coli* and *Staphylococcus* indicate that at least 10% of the isolates exhibited intermediate sensitivity (12).
[b] Resistant inhibition zones (12).
[c] CIPARS — Canadian Integrated Program for Antimicrobial Resistance Surveillance, data from chicken isolates submitted to Canadian diagnostic laboratories in 2008 (1).
[d] Minimum inhibitory concentrations (MICs) obtained with CVM1AGNF plates, Sensititre®, Trek Diagnostic System. Clinical breakpoints were used (1).
[e] Animal Health Laboratory — diagnostic submissions, Ontario, Canada in 2005 (15).
[f] MICs obtained with plates custom-made for AHL by Trek Diagnostic System. Epidemiological breakpoints were used (15).
[g] Roman numerals I to III indicate the ranking of antimicrobials based on importance in human medicine as outlined by the Veterinary Drugs Directorate, Health Canada (9).
— = not tested.

be extra-label. Numerous feed-grade antimicrobials provide inexpensive therapeutic alternatives; however, other routes of administration are recommended, as feed consumption during neonatal stages is insufficient to achieve adequate minimum inhibitory concentrations (MICs) (5).

In growing birds, arthritis and airsacculitis require therapeutic interventions. The value of the individual bird, most effective route, and practicality are taken into consideration; thus, mass medication via water and feed are generally the most common routes of administration during the growing period (23,24,30). For therapy of arthritis, the CVMA-pug recommends potentiated sulfonamides. For airsacculitis therapy, the CVMA-pug suggests the use of the same antimicrobials plus others, such as amoxicillin, tetracyclines, and tetracycline-neomycin (5). For enteritis, a less commonly recognized *E. coli* condition (20), neomycin and tetracyclines are typically recommended (23).

The antimicrobial susceptibility patterns of Canadian *E. coli* isolates *in-vitro* (Table 4) indicate significant changes when compared to both *in-vitro* and *in-vivo* data from peer-reviewed literature (Table 3). For example, in Québec, high prevalence of resistance to ceftiofur, ampicillin, gentamicin, and tetracycline and lower prevalence of resistance to enrofloxacin, neomycin, and trimethoprim-sulfas (Table 4) were observed in clinical *E. coli* isolates in 2010 (12). These clinical AMR data were aggregates of all avian species (66% of these were from chickens) and AMU history are lacking. Other available data such as AMR in abattoir isolates indicate susceptibility to gentamicin and trimethoprim-sulfa (1), but there are limitations for the use of these drugs in chicks: gentamicin requires a long withdrawal period and there are no trimethoprim-sulfonamide preparations available for hatchery applications. However, the potentiated sulfas have been used to treat older birds (38,39), thus, extending their indications to include treatment of CRD and arthritis in broilers could be explored by manufacturers.

Characterization of APEC strains and AMR testing are not routinely conducted by CIPARS or any diagnostic laboratories across Canada. The AMR patterns of APEC strains, from 2 studies conducted in the US and China (40), indicate that APEC have become resistant to most antimicrobials currently used in poultry. Further characterization of APEC isolates from healthy birds and clinical cases and their AMU history are important to fully understand the impact of AMU practices on AMR of this important broiler pathogen.

Clostridium perfringens

Necrotic enteritis (NE) is the most important of the clostridial diseases affecting broilers; current economic consequences of this disease are largely driven by the costs of prevention (41). The

Table 5. Review of antimicrobials for treatment of *Clostridium perfringens* infections in broiler chickens

	Antimicrobial[a]	Type of study	*n*[b]	Duration and dose	Route	Comments	Year (Reference)
I[c]	No drugs cited						
II	Amoxicillin	*In-vivo*/efficacy	240	4 days: 50–150 g/1000 L	PO (water)	↓ lesions	2010 (54)
	Lincomycin	*In-vivo*/efficacy	240	4 days: 50–150 g/1000 L	PO (water)	↓ lesions	2010 (54)
	Penicillin G potassium	*In-vivo*/efficacy	1600	5 days: 0.2–0.4 g/L	PO (water)	↓ mortality/lesions	2008 (52)
	Tylosin	*In-vivo*/efficacy	240	4 days: 100–200 g/1000 L	PO (water)	↓ lesions	2010 (54)
		In-vivo/efficacy	2000	7 days: 50–300 ppm	PO (feed)	↓ mortality/lesions	2001 (53)
	Virginiamycin	*In-vivo*/efficacy	280	35 days: 5–40 g/ton	PO (feed)	↓ mortality/lesions	1982 (88)
III	Bacitracin methylene disalicylate (BMD)	*In-vivo*/efficacy	2000	41 days: 55 ppm	PO (feed)	↓ mortality/lesions	2003 (49)
	Bacitracin, Zinc	*In-vivo*/efficacy for prevention and treatment	1122	100 mg/gal prevention, 200–400 mg/gal treatment	PO (water)	Prevention in low dose, ↓ mortality ↓ lesions in higher doses	1978 (50)
	Chlortetracycline	*In-vitro*/intestinal isolates from broilers	47 isolates	n/a[d]	n/a	Active at very low MIC[e] but low level acquired resistance observed	2004 (89)
	Oxytetracycline	*In-vitro*/intestinal isolates from broilers	47 isolates	n/a	n/a	Active at very low MIC low level acquired resistance observed	2004 (89)
IV	Lasalocid	*In-vivo*/efficacy	189	Up to 24 d: 75 ppm	PO (feed)	↓ lesions	2010 (54)
	Maduramicin	*In-vivo*/efficacy	189	Up to 24 d: 5 ppm	PO (feed)	moderate ↓ lesions	2010 (54)
	Narasin (Nar)	*In-vivo*/efficacy *In-vivo*/efficacy	189 2000	Up to 24 d: 70 ppm Up to 41 d: 70 ppm	PO (feed) PO (feed)	↓ lesions ↓ mortality/lesions	2010 (54) 2001 (51)
	Narasin + BMD	*In-vivo*/efficacy	2000	Up to 41 d: 70 ppm (Nar) + 55 ppm (BMD)	PO (feed)	↓ mortality/lesions	2001 (51)
	Narasin + nicarbazine (Nic)	*In-vivo*/efficacy	189	Up to 24 d: 50 ppm (Nar) + 50 ppm (Nic)	PO (feed)	moderate ↓ lesions	2010 (54)
	Salinomycin	*In-vivo*/efficacy	189	Up to 24 d: 70 ppm	PO (feed)	↓ lesions	2010 (54)

PO — *per os* (by mouth).
[a] Cited by various authors and are available in Canada for veterinary use.
[b] Otherwise indicated, "*n*" refers to the total number of animals used in the study.
[c] Roman numerals I to IV indicate the ranking of antimicrobials based on importance in human medicine as outlined by the Veterinary Drugs Directorate, Health Canada (9).
[d] n/a — not applicable, *in-vitro* test only.
[e] MIC — minimum inhibitory concentration.

disease has been associated with a novel toxin, NetB, produced by α toxin-producing *C. perfringens* type A (42). The public health impact of *C. perfringens* responsible for NE is low (43), but the proliferation of enterotoxigenic strains in chickens is a potential threat to human health, given that the trend in poultry AMU has been declining in some parts of the world (41). In Canada, enterotoxigenic strains have not been detected in retail chicken (44) or in broiler clinical cases (15). The current prevalence of NE in Canadian broiler flocks is unknown, but NE was diagnosed in 4% of broiler flocks and 8% of all broiler laboratory submissions between 1969 and 1971 (45) and has remained one of the diseases frequently diagnosed by the Animal Health Laboratory (AHL) (13,15) and private practitioners (46) in Ontario.

Antimicrobial growth promotants (AGPs) have been used in poultry to prevent infections and promote growth (47). Mandatory and/or voluntarily withdrawal of AGPs has been implemented in other countries; in Canada, the VDD has prioritized the evaluation of AGP claims to manage public health risks arising from animal use (48). The AGPs bacitracin and virginiamycin are listed in the CMIB for growth promotion/improved feed efficiency in broilers and for the control of NE (8).

The antimicrobials of choice for *C. perfringens* therapy are benzylpenicillin, followed by aminopenicillins, then tylosin (23). Table 5 summarizes 14 antimicrobials by VDD Category and based on the choices above, plus drugs listed in other references (23,24). Information was obtained from peer-reviewed publications from 1978 to 2010 conducted largely in Belgium and Canada investigating their clinical or microbiological efficacy. Excluded from the list are drugs that have been withdrawn or

Table 6. Review of antimicrobials for treatment of *Staphylococcus* spp. infections in broiler chickens

	Antimicrobial[a]	Type of study	*n*[b]	Comments	Year (Reference)
I[c]	Ceftiofur	*In-vitro*/diagnostic isolates from broilers	154	Active against coagulase-staphylococci	1996 (90)
	Enrofloxacin	*In-vitro*/diagnostic isolates from broilers	154	Active against coagulase + and − staphylococci	1996 (90)
II	Ampicillin	*In-vitro*/enteric isolates from broilers	923	Wide MIC[e] range	1978 (66)
	Erythromycin (1 wk, 102 mg/L water)	*In-vivo*/efficacy trial, skin exposure model in broilers	150	↓ bacterial recovery	1975 (65)
		In-vitro/diagnostic isolates from broilers	154	Wide MIC range, limited activity	1996 (90)
	Gentamicin	*In-vitro*/diagnostic isolates from broilers	154	Wide MIC range, limited activity	1996 (90)
		In-vitro/diagnostic isolates from broilers	77	Most isolates susceptible	2003 (67)
	Lincomycin (1 wk, 200 ppm of feed)	*In-vivo*/efficacy trial, skin exposure model in broilers	150	↓ bacterial recovery	1975 (65)
		In-vitro/diagnostic isolates from broilers	154	Wide MIC range, limited activity	1996 (90)
	Penicillin G potassium	*In-vitro*/diagnostic isolates from broilers	154	Wide MIC range, limited activity	1996 (90)
		In-vitro/enteric isolates from broilers	923	Wide MIC range	1978 (66)
	Streptomycin	*In-vitro*/enteric isolates from broilers	923	Only 32% of isolates inhibited	1978 (66)
		In-vitro/diagnostic isolates from broilers	77	Most isolates susceptible	2003 (67)
	Tylosin (1 wk, 200 ppm of feed)	*In-vivo*/efficacy trial, skin exposure model in broilers	150	↓ bacterial recovery	1975 (65)
III	Chlortetracycline (1 wk, 200 ppm of feed)	*In-vivo*/efficacy trial, skin exposure model in broilers	150	↓ bacterial recovery	1975 (65)
	Spectinomycin	*In-vitro*/diagnostic isolates from broilers	154	Wide MIC range, limited activity	1996 (90)
	Tetracycline	*In-vitro*/diagnostic isolates from broilers	154	Wide MIC range, limited activity	1996 (90)
IV	No drugs cited				
n/a[d]	Novobiocin (1 wk, 350 ppm of feed)	*In-vivo*/efficacy trial, skin exposure model in broilers	150	↓ bacterial recovery	1975 (65)

[a] Cited by various authors and are available in Canada for veterinary use.
[b] Number of animals in *in-vivo* studies or number of isolates in *in-vitro* studies.
[c] Roman numerals I to IV indicate the ranking of antimicrobials based on importance in human medicine as outlined by the Veterinary Drugs Directorate, Health Canada (9).
[d] n/a — not applicable, *in-vitro* test only.
[e] MIC — minimum inhibitory concentration.

never used in Canada (e.g., avoparcin and avilamycin). Available drugs in Canada for NE therapy are classified under the VDD's Categories II to IV; no Category I drug was cited in the literature, though of note, streptogramins (e.g., virginiamycin) were recently re-categorized from Category I to II (9). Most of the cited antimicrobials are for OTC/label use but bacitracin and virginiamycin are ELDU if used in dosages higher than the approved prophylactic dose. The CVMA-pug included lincomycin, neomycin, penicillin, tylosin, bacitracin, and tetracycline, plus trimethoprim-sulfadiazine (though no *in-vivo/in-vitro* information was found for this drug combination) (Table 2). There are also 6 drugs listed in the CMIB for feed medication: 4 with indications for NE (bacitracin, narasin, tylosin, virginiamycin), and 2 with indications for non-specific enteritis (chlortetracycline and oxytetracycline). Bacitracin (49,50), narasin (51), penicillin (52), and tylosin (53) have been documented to be efficacious under Canadian conditions. These antimicrobials have short residue withdrawal periods in-feed and water (1 d or less) (7) based on maximum residue limits (MRLs) determined to be safe for humans and animals (48). Susceptibility profiles could be considered in establishing (or updating current) MRLs, in addition to public health-driven thresholds for residues, in light of the AMR observed in *C. perfringens* (15,16) and other bacteria (1,3).

Coccidiostats are also used to control NE because of their inherent anticlostridial activity (54). Narasin, an ionophore, is the only drug in Canada that has a claim for NE (8). The coccidiostats belong to the VDD's Category IV and are currently not used in human medicine (9), though recently, their antiviral property has been investigated (55). Studies suggest that diets supplemented with coccidiostats, such as salinomycin in broilers, modulate AMR and virulence determinants in certain strains of *E. coli* (56,57), but more investigations are required to assess the impact of these strains on animal/human health.

Little is known about the AMR profile of *C. perfringens* in broilers in Canada, as *C. perfringens* is not routinely monitored. However, in a study conducted in Ontario from 2005 to 2007, *C. perfringens* isolates from conventionally raised broilers were

100% resistant to bacitracin, compared with 34% resistance in isolates from antimicrobial-free-raised broilers (16). Further, *in-vitro* investigation of Ontario clinical isolates in 2005 confirmed high prevalence (25% to 64%) of resistance to bacitracin, virginiamycin, and tetracycline (Table 4) (15). Resistance of *C. perfringens* to these drugs has also been reported in European countries (58). Given the positive impact of the antimicrobial bacitracin on host response against NE (59) and emerging AMR, there is a need to preserve the efficacy of bacitracin and other efficacious drugs.

Since Canadian data on NE prevalence and AMU/R are sparse, this organism should be included in surveillance programs of animal pathogens to guide veterinarians in their therapeutic approaches, to inform policies related to AMU, and to direct research towards novel alternatives.

Staphylococcus

Staphylococcus spp. have been associated with yolk sac infection and omphalitis in newly hatched chicks, and septicemia, osteomyelitis, arthritis, synovitis, and gangrenous dermatitis in older birds (60). These conditions impact performance, condemnation rates, and welfare. No reports have linked clinical disease in Canadian broilers to occupationally transmitted human disease; rather, the public health threat is related to the consumption of meats contaminated with enterotoxigenic *S. aureus* strains causing food poisoning (61) and contact with meat contaminated with methicillin-resistant *S. aureus* (MRSA) (62). The organism is frequently isolated from avian clinical cases in Québec (12), but the prevalence rate is unknown.

Staphylococcal septicemia could lead to joint infections/arthritis (63). Joint infections in broilers are therapeutically challenging. Therapeutic schemes in mammalian species could include surgical removal of sequestrae, prolonged parenteral antimicrobial therapy, and local antimicrobial administrations (64) but these interventions are impractical for broilers because of the low economic value of the individual bird (24). Management efforts to reduce septicemia and joint infections include culling of chicks with unhealed navels [i.e., entry point for *Staphylococcus* (60)], good litter quality, and removal of potentially abrasive surfaces at the barn.

First choice antimicrobials include penicillins and potentiated sulfonamides, followed by aminopenicillins and tetracyclines, then macrolides (e.g., erythromycin) (23). Other drugs were also suggested, including novobiocin, spectinomycin, and streptomycin (24). Table 6 summarizes data on 14 antimicrobials by VDD Category. The contributing studies were conducted mainly in Belgium and the US from 1975 to 2003, investigating the susceptibility patterns of isolates from broiler diagnostic cases. Very few *in-vivo* studies on antimicrobial efficacy were found, though 1 skin exposure study (i.e., proposed mechanism of entry point of *Staphylococcus* leading to systemic infections) was noted (65). Currently available drugs for staphylococcal therapy in Canada are classified under VDD's Categories I to III, and no drugs cited were in VDD's Category IV. Most of these antimicrobials are available in Canada but are largely ELDU, except for erythromycin and the tetracyclines which are for OTC/label use. The CVMA-pug lists 5 drugs for *S. aureus* arthritis: erythromycin, lincomycin-spectinomycin, ormethoprim-sulfadimethoxine (no *in-vitro* or *in-vivo* information for this drug combination), penicillin, and tetracycline (Table 2). Novobiocin, an aminocoumarin antibiotic, was originally licensed for staphylococcal therapy in turkeys but is no longer included in the CVP. Lincomycin and lincomycin-spectinomycin by SC injection have been investigated (37), but this route of administration is ELDU for these products.

Susceptibility testing of clinical isolates and assessment of the success of previous treatment are recommended, as some antimicrobials (e.g., penicillins) are known to be efficacious against *Staphylococcus* but have been documented to have wide MIC distribution ranges *in-vitro* (66). *Staphylococcus* AMR data in Canada is limited and often presented as an aggregate for all avian isolates. In Québec, some resistance to enrofloxacin, ampicillin, neomycin, and tetracycline was noted in 2010 among clinical avian isolates (Table 4) (12). In the US, clinical isolates collected from 1998 to 2000 exhibited resistance to tetracycline, lincomycin, and erythromycin, but were susceptible to gentamicin and streptomycin (67). In Denmark, isolates from sick birds from 1994 to 1998 exhibited resistance to ciprofloxacin, sulphamethoxazole, and erythromycin but were susceptible to most antimicrobials tested (68). Given the animal health and welfare impacts of *Staphylococcus,* this organism should be included in the surveillance of animal pathogens. The human health impact of poultry-derived staphylococci in high-risk groups (i.e., poultry workers) also needs to be monitored.

Enterococcus cecorum

Enterococci are normal inhabitants of the human and animal gut flora, but some cause disease in humans and animals (69). Species found in animals *(*i.e., *E. durans)* could also transfer AMR determinants to species found in humans (i.e., *E. faecium*) (70). Given their predisposition to acquire resistance genes, enterococci are used to monitor AMR (1,3). In poultry, *E. cecorum* has been associated with vertebral canal stenosis (VCS) or osteomyelitis, which occurs more frequently in male birds (71,72). In Ontario, VCS was first diagnosed by the AHL in 2008 (6). An increase in diagnostic submissions of VCS in Ontario (6) has been associated with the emergence of a homogeneous major clonal lineage of *E. cecorum,* genetically unrelated to commensal *E. cecorum* (73).

Literature describing the therapeutic approaches to VCS in Canada is lacking. In a recent Canadian study, clinical isolates were susceptible to penicillin and resistant to tetracycline, bacitracin, erythromycin, and streptomycin and had elevated MIC's to gentamicin and enrofloxacin (73). Isolates in Belgium also exhibited susceptibility and resistance patterns to the same antimicrobials/class of antimicrobials (70). Further investigation is required to understand the epidemiology (e.g., male versus female predilection, management, AMU practices) and virulence attributes of the *E. cecorum* clone responsible for VCS, and to understand how this clone localizes to extra-intestinal sites. The public health significance also needs to be assessed (e.g., transfer of AMR determinants to human enterococci), given their current AMR patterns, particularly to enrofloxacin.

This organism should also be included in national surveillance of animal pathogens.

Salmonella

Salmonellosis in chickens is rare, and if birds are infected with certain serovars and phage types, disease that is clinically similar to colibacillosis may occur (74). In Canada, the recovery rate of *Salmonella* from abattoir chickens increased from 16% in 2002 to 28% in 2008 (1). Similarly in the US, the prevalence of *Salmonella* also increased between 2007 and 2009 in retail chicken (3), but it is unclear if the increases seen in both countries are coincidental or if the exchange of poultry products played a role (2).

Enrofloxacin, in combination with competitive exclusion products has been effective in eliminating *S.* Enteritidis from experimentally infected chicks (75), but if used in broiler breeders (i.e., a potential source), this may result in the transmission of fluoroquinolone-resistant *Campylobacter* in broilers (76). Other attempts to treat salmonellosis have proven unsuccessful. For example, proliferation of *Salmonella* in the gut occurred after neomycin therapy (77) and killing of intracellular *Salmonella* (i.e., *in-vitro*) failed with gentamicin treatment (78). Ceftiofur (79) has also been investigated *in-vitro* against *Salmonella,* but as previously described, its use in poultry has raised a public health concern in North America (1,19,35,36). Only amoxicillin has a claim in Canada for *Salmonella* in broilers by oral administration. The CVMA-pug and CMIB have not included salmonellosis in the list of diseases or conditions indicated for antimicrobial therapy.

Antimicrobial use has not been recommended as an approach to control this pathogen in poultry. In Europe, strict regulations discourage the use of antimicrobials in controlling *Salmonella* infections [e.g., Commission Regulation (EC) No 1177/2006]. Maintenance of negative disease status in multiplier flocks is important for *Salmonella* control and is best carried out by eradication of positive flocks (74). In Canada, the eradication of flocks positive with *S.* Enteritidis and *S.* Typhimurium DT104 is not covered under any federal compensation program, though an insurance policy that covers losses due to flock eradication is available in some provinces (80).

There is ongoing evidence that chickens are frequently contaminated with *Salmonella,* including resistant strains (Table 4) (1–3). Because of the AMU limitations for treating salmonellosis, industry-level operational factors such as enhanced prevention/eradication program in broiler breeders, establishing quality thresholds for hatching egg/chick for domestic and imported sources, and enhanced farm/hatchery hatching egg care practices such as those described for *E. coli* are recommended to reduce infection with *Salmonella.*

Conclusions

This review has integrated currently available information on AMU for the therapy of commonly diagnosed bacterial diseases in Canadian broiler flocks. This review found that first, Canadian AMU guidelines exist for treating the common bacterial diseases of broilers and antimicrobials are available to producers/veterinarians for administration to their flocks. However, in some cases these antimicrobials are available OTC (thus may be administered without veterinary oversight) or have to be prescribed in an ELDU manner (thus may not have been reviewed for human safety aspects related to AMR). The authors recognize the limitations and implications of the various therapeutic approaches on AMR. As examples, in clinical infections, sick birds may exhibit depression, inappetence, and immobility, thus affecting their ability to consume medications administered via food or water, resulting in variations in antimicrobial exposures (i.e., over and under-dosing), potentially impacting selective pressure for AMR. Consequently, prudent AMU practices are reliant on the veterinarian's assessment of the clinical condition and should consider animal health, welfare, and public health concerns. Secondly, prevalence information regarding broiler diseases requiring antimicrobial therapy is largely unknown or unavailable through publicly accessible means. Third, there is no quantitative information available regarding antimicrobials used in broilers in Canada (i.e., OTC, prescription, OUI, API's), affecting interpretation of observed resistance patterns. And finally, AMR has emerged between 1975 to 2011 in broiler pathogens and in indicator bacteria, but the data are sparse, thus firm conclusions regarding the implications of AMR in broiler pathogens on treatment efficacy cannot be made.

In conclusion, the authors recommend implementation of an on-going surveillance program for AMU/R that integrates disease prevalence data from diagnostic cases (i.e., the main driver of AMU) and farm/hatchery-level data to address animal and public health concerns related to the use of antimicrobials. The heterogeneity of poultry sources, domestic and imported, poses a challenge for source attribution of AMR. This information gap may be filled by additional hatchery AMU data and purposive sampling of both domestic and imported chicks for AMR testing. To address emerging AMR concerns with drugs of very high importance to human medicine, the use of drugs of lesser importance to human medicine (i.e., lower category drugs) should be explored for both hatchery and farm use. Additionally, AMU practices (e.g., prescription, OTC, ELDU, OUI, and API) should be re-evaluated and monitored, and farm food safety programs should be enhanced to reduce diseases that drive AMU/R. Chicken is an important commodity in Canada; integrated surveillance that informs both prudent AMU practices and human health risk analysis are essential to the preservation of efficacious antimicrobials important to veterinary and human medicine. CVJ

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