

Commentary Commentaire

Stewardship of antimicrobial drugs in animals in Canada: How are we doing?

Ad-Hoc Committee for Antimicrobial Stewardship in Canadian Agriculture and Veterinary Medicine

Modern medicine relies heavily on antibiotics, the availability of which has largely been taken for granted. The emergence of antimicrobial resistance is a serious and ever-increasing global threat to our ability to control bacterial infection, and has been characterized as a global crisis. The use of antibiotics in animals is recognized to contribute to the problem of resistance, although the scale is still not clear. Since 1999, there have been innumerable international and national reports about appropriate use of antibiotics in humans and in animals (1–4). There have been 3 national conferences in Canada on use of antibiotics in animals (5–7), and a landmark report to Health Canada in 2002 on how to improve agricultural use of antibiotics (8).

The purpose of the present report is to comment on progress in the last decade, and to identify and prioritize areas that still need work to allow Canada to meet international or national recommendations for good stewardship practices for antimicrobial drug use in animals.

Ad-hoc committee

The purpose of the Ad-Hoc Committee for Antimicrobial Stewardship in Agriculture and Veterinary Medicine is to provide leadership through continued discussion, communication, and advocacy on action points identified by participants at the Toronto 2011 Conference on this topic (7). The intent is to promote the development or enhancement of antimicrobial stewardship initiatives at the national, provincial, regional, and institutional levels. The Committee is comprised

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The Ad-Hoc Committee for Antimicrobial Stewardship in Canadian Agriculture and Veterinary Medicine includes Marie Archambault, Patrick Boerlin, John Campbell, Melissa Dumont, Jim Hutchinson, Duane Landals, J. McClure, Scott McEwen, John Prescott (Co-Chair), Joe Rubin, Durda Slavic, Barry Stemshorn, Warren Skippon, Scott Weese, Jean Szkotnicki (Co-Chair), and Ed Topp.

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of non-governmental individuals who served on the Conference Organizing Committee for the 2011 Antimicrobial Stewardship in Agriculture and Veterinary Medicine with the addition of several individuals following that Conference. Government officials who served on the Organizing Committee for the 2011 Conference may be observers to the work of the Ad-Hoc Committee. "Voting" members of the Ad-Hoc Committee come from veterinary academia, veterinary associations, animal health diagnosis, the animal health industry, human medicine, and environmental science, and have a commitment to improving how antibiotics are used in animals and humans in Canada. The Committee works through a list server and has bi-monthly 1-hour teleconferences.

In 2013 the co-chairs submitted a petition to the federal Ministers of Health, Agriculture and Agri-Food, and Public Safety and Emergency Preparedness through the Commissioner of Environment and Sustainable Development seeking action to address long-standing gaps in federal legislation (9).

Assessment approach

The assessment provided a structured approach for the committee to document its views of progress in Canada against major recommendations arising from: The World Health Organization report on Global Strategy for Containment of Antimicrobial Resistance (2000) (1); Health Canada's Committee's 2002 Report: Uses of antimicrobials in food animals in Canada, major recommendations (8); the 2011 national Antimicrobial Stewardship conference held in Toronto (7); and the major recommendations of OIE Global Conference on responsible and prudent use of antimicrobial agents for animals, 2013 (3). As well, consideration was given to harmonization with initiatives to prevent antimicrobial resistance in the United States (10). The Committee agreed on the major recommendations to be ranked, but assessors were given the opportunity during the individual ranking process to include other (more minor) recommendations from the World Health Organization report on Global Principles for the Containment of Antimicrobial Resistance in Animals Intended for Food (2) and the Health Canada's Committee's 2002 Report (8). Assessment was voluntary and done without attribution to individual members. In addition to providing a rank, assessors were also asked to assign a priority to the recommendations.

The assessment was based on assigning a rank (A, B, C, D, E, or INC) and a priority range (1 to 17) for each rubric. Rank interpretation was as follows: A = Canadian practice fully meets

or exceeds international standards or Canadian recommendations; B = Canadian practice approaches international standards or Canadian recommendations, shows evidence of understanding and addressing the stewardship issues involved and has a trajectory to meet or exceed international standards or Canadian recommendations; C = Canadian practice displays an adequate and general understanding of the stewardship issues involved, but requires improvement to fully meet or exceed international standards or Canadian recommendations; D = Canadian practice displays a barely satisfactory understanding of the stewardship issues involved, and requires marked improvement to meet or exceed international standards or Canadian recommendations; F = Canadian practice is inadequate, displays an unsatisfactory understanding of the stewardship issues involved, and fails to address in any significant way international standards or Canadian recommendations; INC = no data are available. The ranking assigned was that most frequently assigned by the group; the priority was based on the mean priority assigned by the group. Comments from the different scorers were inserted “verbatim” into the final ranked and scored recommendations, and provided to the group with no editorializing. The comments now provided in this summary represent a brief selected summary of the rationale provided by the assessors and includes the range of opinions expressed.

Assessment rankings and priorities

Results of the assessment of the priority for future focus to improve antimicrobial stewardship in animals in Canada, and of the assessment of current progress against international and national recommendations are given in Table 1. Seven of the non-governmental members of the Committee provided assessment and comments.

Additional comments not relating to the ranking of recommendations were about proposals to decouple veterinary prescribing and dispensing. This needs to be examined more closely, since the current veterinary practice business model is based in part on an income stream from antimicrobial sales.

Despite the overall poor assessment of Canada’s stewardship of antimicrobial drugs in animals (Table 1), progress has been made in the more than a decade since the report to Health Canada (8). The most notable progress recognized by respondents has been the development and work of the Canadian Integrated Program for Antimicrobial Surveillance (CIPARS), which has achieved international recognition for the quality of its work. Respondents also favorably noted, by “B” rankings, the progress at the national level in general and practice-specific antibiotic use guidelines by the CVMA, as well as the “pre-licensing safety evaluation in relation to human use” of new antibiotics by Health Canada. Some provincial veterinary licensing bodies, led by Quebec, have established or are developing mandatory continuing education programs on antimicrobial stewardship; efforts underway to improve collaboration amongst Canada’s veterinary licensing bodies could provide a foundation for progress in this area. In response to Petition #342 the Minister of Health stated that Health Canada’s modernization agenda would include discussion of changes in regulations relating to the importation of active pharmaceutical

ingredients (API) and pharmaceuticals for “own use” (OUI) (9). We have also reviewed and supported regulatory measures proposed by Health Canada officials in an unpublished consultation document of March 2013; these measures included a permitting regimen for OUI with exclusion of important antimicrobials, and a licensing requirement for establishments that process API. These measures would be important steps forward. Despite progress in resistance monitoring through the work of CIPARS, this recommendation was assessed most frequently as a “C” for progress because of the apparent inability under Canada’s federal-provincial jurisdictional divide to take national corrective action if a significant resistance problem is identified. Resistance monitoring remains a high priority.

The current jurisdictionally fragmented regulatory framework, in which the **federal** authorities regulate sale of antimicrobials but **provincial** authorities regulate the use of these products in varying ways, has enormous impact on the ability to control antibiotic use in animals in Canada. This was a recurring theme in the commentary, and seems to prevent this country from being able to meet international standards (1–4) or even national recommendations (8) for improved use of antibiotics. “Fs” were assigned to signal the lack of progress in addressing long-standing national recommendations (8) to tighten controls on the importation of antimicrobials for API and OUI, and compounding. One respondent commented that, in regard to federal authority, “where there is a will there is a way.” Let us hope that it will not take a disaster to drive the needed regulatory changes, although from some perspectives the emergence and spread of resistance in human pathogens is a potential disaster for humanity. The top 8 of the ranked priorities all relate to regulatory issues; clearly there has to be movement in national regulation of antibiotic use in animals if Canada is to meet international standards. We call on the federal government to show leadership within its own spheres of authority while working in collaboration with provinces to take a serious effort to build nationally coordinated approaches.

“D’s” (“requires marked improvements”) were assigned to terminating growth promoters, making antibiotics “prescription only” for food animals, developing extra-label drug use policies that don’t endanger human health, and the related recommendation for following OIE guidelines about fluoroquinolone and third-generation cephalosporin use, and promoting alternatives to antibiotics or improving antibiotic use generally. In regard to recommendations about terminating the use of antibiotics of significance to humans as growth promoters, this is a complex issue since there is confusion between the use of antibiotics for their growth promotional value and their use in specific disease prophylaxis. In part this confusion is because some of the terminology and approved claims go back decades to the early days of antibiotics; most antibiotics are not actually used for growth promotional purposes per se, but rather for disease prophylaxis. Nevertheless, the removal of use of antibiotics of significance in human medicine specifically for growth promotion in animals is required if Canada is to meet international standards for antimicrobial stewardship, and would harmonize with developments in the United States (9).

Table 1. Priority assignment for future focus and summary of ranking of Canadian progress in meeting international standards of, or national recommendations for, good stewardship practices for antimicrobial drug use in Canadian agriculture and veterinary medicine

Recommendation	Priority: rank	Selected comments associated with the recommendations justifying ranking or scoring
Create a national system to monitor use in food animals (3,4,7,8)	1: C	Canada has no reliable system to monitor antimicrobial drug use in animals. The recent provision of 2011 sales data to the Canadian Integrated Program for Antimicrobial Surveillance (CIPARS) by the Canadian Animal Health Institute (CAHI) of quantities of antibiotic sold by its members based on drug class, practice type (food animal, companion animal) and Province was regarded as an important development, but also as “minimal” information, in part since it is sales and not use data. Unregulated sources (active pharmaceutical ingredients, APIs; Own Use) are not included in these data.
Terminate growth promoters if drugs used in humans (3,4,8,9, US harmonization issue)	2: D	One respondent commented that implementing this recommendation would “require a complete overhaul of the <i>Feeds Act</i> and the Medicated Ingredients Brochure process before we can eliminate growth promotion claims and replace them with specific medical indications”.
Stop the importation, sale and use of antimicrobials not evaluated and registered by Health Canada (“own use,” “APIs”) (3,7,8; US harmonization issue)	3: F	The lack of progress on this recommendation was regarded as “a continuing international and national embarrassment.” It “has been studied for 15+ years and still no effective regulatory solution has come to light. Direct use of APIs in animals is a significant risk to animal and public health/food safety, not to mention a significant risk to trade.” “There is understanding by the federal government but it has no legal authority to address own use or API use.”
Monitor resistance and take corrective action if needed (4,8)	4: C	Respondents recognized the value of the monitoring currently in place through CIPARS but were unanimous in their frustration at the limited federal authority for oversight which appears to impede ability to take corrective action.
Prescription only of antibiotics for food animals (4,8)	5: D	Prescription only “would bring us to international standards and could address the use recommendation by easing reporting.” “There is not an understanding that Rx only does not necessarily mean prudent use.” “The Quebec prescription-only model needs to be more closely examined as a viable template for provincial oversight;” but “We need to analyse usage in Quebec data given that CAHI data suggest use is highest in Quebec — are we to take it that veterinarians are over-prescribing?”
Develop an extra-label use policy, which ensures no endangerment to human health. Include ability to prohibit extra-label use of specific drugs of critical importance to human health (4,7; US harmonization issue)	6: D	“We have some very non-specific guidelines, nothing like <i>Animal Medicine Drug Use Clarification Act</i> (AMDUCA). The problem with extra-label guidelines that prohibit extra-label use is that extra-label drug use (ELDU) can be the most “judicious use” of that drug;” “A firm policy on ELDU at a national level is essential for provincial regulators to regulate use.” “There is no mechanism for harmonization of provincial policy except through federal policy;” and “there needs to be a national consultative body for provincial veterinary statutory bodies to connect with federal policy.” “Why are we not harmonizing ELDU policy across provinces?”
Follow OIE guidelines re fluoroquinolones and 3rd- and 4th-generation cephalosporins (3)	7: D	“We lack ability to prohibit at the national level if there is a problem;” “Health Canada can’t enforce extra-label use changes;” “The OIE recommendation that ELDU of Category 1 antimicrobials (AMs) be used ‘in agreement with national legislation’ is not possible in Canada, since no such regulatory oversight exists.”
Initiate Veterinary Feed Directive (VFD) to ensure veterinary oversight over use of critically important antimicrobials (9)	8: C	Comments included: “Discussions are beginning — a lot of work ahead with risk gaps needing to be managed e.g., ELDU, API, compounding, dose ranges, added species etc;” “There is a long way to go to get veterinary oversight into feed medications;” “This is still a work in progress in the US; would be good to harmonize.”
Develop national leadership and oversight in Canada; culture of resistance awareness (7)	9: C	Comments noted the lack of a coordinated national effort to control AMR, to link provinces and federal government, and the issue of federal versus provincial jurisdictions. “We have good national awareness but the legislative ability to provide leadership and enforcement is lacking.”
Strengthen veterinary curriculum around antimicrobial resistance and stewardship (3,7)	10: C	“Needs to be an AVMA/CVMA core competency” and “Probably happening, but not coordinated, needs to be an accreditation issue.” “Unfamiliar with how AM stewardship is taught;” “unfamiliar if the CVMA livestock prudent use guidelines are used for teaching purposes or utilized in a clinical setting at vet colleges.”
Veterinary (<i>regulatory</i>) bodies to develop, implement and ensure compliance with ethics and codes of practice, promote CE (3,7)	10: C	“Needs improvement; I would like to think we are all aware of the issues and are doing better. However, there are still differences between provinces and this will require national leadership to harmonize;” “There is an attempt to discuss with other provinces but progress is slow; CVMA, OMVQ, OVMA and others have shown leadership;” “Should be part of Quality Assurance and accreditation for practitioners;” “Vet bodies are hampered by conflicts of interest.”
Ensure oversight of compounding and that manufacturing is not being done under the guise of compounding (US harmonization issue)	10: F	“Not satisfied that this is being dealt with;” “This is important for many reasons beyond AMR issues;” “There needs to be federal policy in this regard. It is inadequate to say that compounding is simply practice and therefore provincially regulated. The provinces regulate how compounding is done but not what products might be compounded or where they are sourced. We cannot control interprovincial movement of compounded products;” “Nothing can be done here until fed regulations around API importation are tightened.”
Pre-licensing safety evaluation re human AMR (4,8)	13: B	“Low priority because done;” “The Veterinary Drug Directorate is doing what can be done;” “Is being done somewhat with newer drugs but not the older ones.”

Table 1. Priority assignment for future focus and summary of ranking of Canadian progress in meeting international standards of, or national recommendations for, good stewardship practices for antimicrobial drug use in Canadian agriculture and veterinary medicine (continued)

Promote alternatives to antibiotics for animals; improved use of antibiotics; agricultural practices; diagnostic tests; global and regional cooperation for responsible and prudent use (4,7)	14: D	“There are a number of initiatives, but sense it lacks the thoroughness and rigor that is required;” “Market driven could be important — recent advertising by a major retail chain claiming their meat is free of antibiotics;” “This is a fundamental principal of prudent use, the need to have herd/flock health management program in place to minimize the use of AMs.” “Veterinarians have shown significant leadership in this area, but needs to be taken to another level (e.g., reduce/eliminate growth promotion AMs).”
Develop prudent use guidelines for veterinarians to improve use in food animals (4)	15: B	Respondents recognized that considerable effort had gone into guideline development by the CVMA, and ranked this highly among the rank recommendations, but were uncertain about uptake and implementation. General guidelines were regarded as having little impact, and practice use guidelines as having more value.
Sustained funding for CgFARAD (7)	16: B-D	Respondents were divided on this recommendation since some saw it relating to residue rather than to resistance avoidance.
Availability of licensed antibiotics for “Minor use-Minor Species” (7)	17: C (2 Fs)	Respondents were also divided on this recommendation, since “may not be the big player in AMR, especially if used judiciously. After all they are “minor species;” However, “If we are to restrict ELDU then labels must be established for Minor Use-Minor Species (MUMS).”

“C’s” (“requires improvement”) were assigned to developing a national system to monitor use in food animals, to monitoring resistance and taking corrective action if needed, to initiating a Veterinary Feed Directive to ensure veterinary oversight on in-feed and water antibiotics (10), to developing national leadership and oversight of antibiotic use in animals, to strengthening the veterinary curriculum around antimicrobial stewardship, to the role of veterinary regulatory bodies in promoting stewardship, and to the problematic lack of licensed antibiotics for “Minor Use-Minor Species.” Development of a robust system to monitor use in food animals would allow Canada to “benchmark” its use of antibiotics in food animal production or in animals generally against other countries, and has value in identifying where there may be overuse (11).

The ranking and prioritization provided here (Table 1) can be criticized as representing the views of a narrow range of respondents. However, the respondents represent those knowledgeable about the use of antibiotics in Canada and about antibiotic resistance who have engaged with the issue for many years. The ranking and prioritization (Table 1) represent a framework around which progress towards meeting international standards and national recommendations could be made. There clearly continues to be need for national dialogue and coordination, and especially for regulatory change if Canada is to address the changes required to meet international standards. Antibiotic stewardship is a complex and challenging issue which will require multiple approaches to improve, but the complex regulatory issues that stand in the way of change in Canada add an additional level of complexity that needs to be resolved.

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