

## **Canadian Situation Regarding the Extra-label Use of Cephalosporin Antimicrobial Drugs in Food-Producing Animals**

Health Canada has noted the publication on January 4, 2012 of the U.S. Food and Drug Administration (FDA)'s Final Rule of the Order Prohibiting Certain Extra-label Use of Cephalosporin Antimicrobial Drugs in Certain Food-Producing Animals. This rule becomes effective on April 5, 2012, but there is a comment period of 60 days. This FDA order is related to the previous order on the same subject that was issued on July 3, 2008 and subsequently revoked on November 26, 2008.

The latest action by FDA is primarily targeted to the prohibition of extra-label use of newer cephalosporins such as the third-generation cephalosporins for disease prevention in major food-producing animal species (e.g., cattle, swine, chickens and turkeys). In comparison with the revoked 2008 order, the new order has narrowed its scope and included certain exemptions, e.g., for not including an older cephalosporin (i.e., the first generation cephalosporin) as well as the therapeutic use in minor species.

In Canada, veterinary cephalosporin drug products are primarily approved to treat infectious diseases in animals. Third-generation cephalosporin products are those considered to be of greatest public health concern in terms of antimicrobial resistance. Relevant to the FDA's order, Health Canada has been working on the same subject for several years. In 2004 Health Canada has categorized the third and fourth-generation cephalosporins as the antimicrobials of Very High Importance in human medicine (Category I). Like in the U.S., there is currently only one third-generation cephalosporin approved for veterinary use in food-producing animals in Canada (ceftiofur). No fourth-generation cephalosporins are approved for use in animals in Canada or the U.S.

In 2006, Health Canada reassessed the approved veterinary third-generation cephalosporin products for human health risks and subsequently required the labels of all such products contain a warning statement that extra-label drug use (ELDU; using drugs in a manner not in accordance with the approved product labels) is not recommended in order to limit the development of antimicrobial resistance. This is consistent with the approach taken by other regulatory organizations and that newly announced by the FDA.

Furthermore, Health Canada has updated in 2008 its policy on ELDU in food-producing animals. This policy has specifically addressed the potential human health risks from antimicrobial resistance associated with the ELDU of medically-important antimicrobials.

The approval for sale and use of drugs in Canada is a multi-jurisdictional issue involving the federal government and the provinces and territories. While Health Canada approves the sale of the drug and sets the conditions of use on the product labels, the use of these products falls under the practice of veterinary medicine. Hence, the provinces and territories play a critical role in implementing Health Canada's recommendations on the restriction of ELDU.

Health Canada has noted that the FDA's order has used the cephalosporin resistance data from the Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) as key supporting evidence. In this regard, the federal governments including Health Canada have been working together with the provincial/territorial authorities as well as food animal industry towards minimizing human health impacts from cephalosporin resistance in foodborne bacteria.

In summary, Health Canada has already taken action to restrict the ELDU of veterinary cephalosporins similar to that taken recently by the FDA. Ongoing concerted efforts are required from federal, provincial and territorial governments, and stakeholders to effectively implement the ELDU restrictions.

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