USING PHARMACOVIGILANCE DATA TO SUPPORT A LIFECYCLE APPROACH FOR REGULATING VETERINARY DRUGS - A CANADIAN APPROACH

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Health Canada is responsible for protecting human and animal health and the safety of Canada's food supply. Working under Health Canada's mandate the Veterinary Drugs Directorate (VDD) evaluates all veterinary drugs sold in Canada and monitors the safety, quality and effectiveness of those drugs.

Legally, the *Food and Drugs Act* and *Regulations* provide the regulatory tool by which the VDD can regulate the evaluation, management and approval of all drugs in Canada. The *Food and Drug Regulations* apply to both human and veterinary drugs and detail the responsibilities of the drug sponsor to get an approval for sale and to maintain that approval. Guidance documents are provided as an aide to assist manufacturers in fulfilling all of the requirements for approval and continued market authorisation of their product.

With the steady urbanisation of Canada's population and a move towards larger farming practices, Canadian livestock production groups have begun to set on-farm food safety programs into place. These programs make the individual producers more accountable for the safety of the products leaving their farms. Ensuring that drug information (e.g. labelling) is up to date and accurate allows producers, and their veterinarians, to make more informed choices with regards to prudent and appropriate veterinary drug use. Through pharmacovigilance, we can monitor for changes in a drug's safety or efficacy profile and respond by keeping the public informed of important changes.

International collaboration plays an ever increasing role in assisting the regulation of veterinary health products in Canada. The ability to use international data in our pharmacovigilance program is an invaluable tool that allows us to draw information from a much larger population than what would be found in Canada alone.

The process of regulating veterinary medicines to ensure human, animal and food safety is complex. In order to ensure the safety, efficacy and prudent use of medications, it is necessary to have a flexible system that allows for regular re-evaluation of veterinary health products. Canada is currently considering a new veterinary drug regulatory framework that will provide this flexibility and will be able to accommodate changes in a drugs lifecycle and emerging technologies in medicine, while maintaining the VDD's mandate: Protecting

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human and animal health and the safety of Canada's food supply.

Health Canada is the federal governmental department responsible for helping Canadians maintain and improve their health. The department is divided into nine Branches and six Agencies whose collective goal is for Canada to be among the countries with the healthiest people in the world.

The Veterinary Drugs Directorate (VDD) is part of the Health Products and Food Branch of Health Canada. To protect human and animal health and the safety of Canada's food supply, the Veterinary Drugs Directorate evaluates and monitors the safety, quality and effectiveness, sets standards, and promotes the prudent use of veterinary drugs administered to food producing and companion animals.

The Directorate is staffed by a multi-disciplinary team of people with skills and experience specific to their job functions. These include program staff with backgrounds in veterinary medicine, biology, microbiology, toxicology, pharmacology, epidemiology, parasitology, animal sciences, aquaculture, environmental health safety and chemistry, IT/ knowledge management, strategic planning, communications, policy, finance and administration.

VDD has authority of the sale and advertising of food, drugs, natural health products, and medical devices in Canada. We cannot, however, direct the practice of veterinary medicine with regards to compounding, appropriate or prudent drug use, or extra-label drug use. These practices are the discretion of the individual veterinarian and their client, and are regulated by the regional veterinary regulatory bodies.

In Canada, the *Food and Drugs Act* and *Food and Drug Regulations* (FDR), and the *Feeds Act* and *Feeds Regulations* (FR), regulate the sale and use of drugs in livestock feeds. The addition of drugs to livestock feed must comply with both sets of legislation, as follows:

Pursuant to the *Feed Regulations*, all medicated livestock feed imported, manufactured or sold in Canada must meet the standards set out in the Canadian Food Inspection Agency's (CFIA) Compendium of Medicating Ingredient Brochures (CMIB), unless the feed is a veterinary prescription feed (a feed that is manufactured pursuant to a veterinary prescription). The CMIB s a listing of drug premixes that have been assigned a Drug Identification Number (DIN) and approved for use in livestock feeds by Health Canada (every drug that is approved for use in Canada is issued a Drug Identification Number).

A medicated feed is exempt from complying with the standards set out in the CMIB only if the medicated feed has been manufactured pursuant to a veterinary prescription and if, amongst other criteria, the source of the medicating ingredient prescribed and used in the medicated feed is in compliance with the *Feed Regulations* and with the conditions set out in the *Food & Drug Regulations*.

A person may sell a medicated feed, pursuant to a written prescription of a veterinary practitioner, if all drugs used in the

medicated feed as medicating ingredients have been approved for sale by Health Canada.

Veterinarians have the responsibility to ensure that drugs prescribed for food-producing animals will not result in harmful or violative residues in food.

The core activities of the VDD include pre-market review of drug submissions from industry, post-market review of approved medications, and policy and regulatory development. While the directorate is divided into five divisions, close communication and exchange of information between the divisions enables efficient use of resources.

As part of the Clinical Evaluation Division within the VDD, the Pharmacovigilance Unit was established in order to monitor safety and efficacy of medications, both nationally and internationally, in order to provide adequate information to consumers on the activities of approved medications. The tool that we employ for communicating information on safety and prudent use, to veterinarians and the public, is the product label.

Human and Veterinary medications differ slightly in the way the information is presented. In Canada, veterinary medications and their packages may be dispensed directly to the producer or consumer and as such, specific information needs to be communicated in a way that is easily understood by the reader.

The development of specific labelling guidelines is important in being able to relay information, in a consistent manner, to those who will be administering the medication. The outer packaging is designed to include important information with regards to the type of medication, dose and administration information, serious cautions or contraindications, and in the case of food producing animals, any information on withdrawal times. Special bulletins regarding serious health concerns, either in humans or in animals, are communicated through "black box" warnings which appear on the outer labelling.

While study and trial data are still important in determining how medications will behave in target and non-target species, the international sharing of post market data enables regulators to see how medications work in real-life settings. Canada's population is quite small (36 million people) as so post market data and adverse event reporting can be scarce. The ability to use post market data from other countries is an invaluable tool that we can make use of when evaluating labelling.

When evaluating a submission from industry, VDD reviews: information regarding chemistry and manufacturing to determine storage conditions; the safety and efficacy of the medication based on study data; residue data to set minimum residue limits, meat and milk withdrawal periods; post market data for adverse reactions. This information is communicated to the public via the product's label.

In Canada, food animal veterinarians are allowed to dispense medications to the producers with whom they have an up to date veterinary-client-patient relationship. If a veterinarian is familiar with a producer's farm they can dispense medications that the producer

can administer themselves. This does not include all veterinary drugs but can include antibiotics, hormones and anti-inflammatories. If it is necessary to use a medication off label (i.e., for a dose / indication / route / species not included on the label) the veterinarian can write a prescription indicating the reason and including appropriate withdrawal times.

With the urbanisation of Canada's population, a shift towards larger farms and more intensive agriculture has resulted. This shift in farm size and husbandry practices has meant a shift in the way medications are being used. Large numbers of animals are raised in large groups. Mixing and moving of animals from different sources present different disease challenges, as well as food safety challenges. Many commodity groups have recognised the need for on-farm food safety programs to help ensure food's safety before it leaves the farm. The on-farm food safety programs vary by commodity group but all of them require the producer to document treatments and animal movements. A producer must document that they have used an appropriate product as per label instructions, or provide a veterinary script to account for off-label use. For this reason upto date and accurate labels on the medications are important.

Changes in disease demographics have resulted in changes in drug use and effectiveness. This has led to the development of a "lifecycle" approach to regulating medications.Currently Health Canada and the VDD are in the process of updating regulations to accommodate this more fluid view of drugs. The Directorate is working to enhance the efficiency of operations and to streamline the review of veterinary drug submissions. At the same time, we are making advancements in the areas of information management and processing, policy development, communications with Canadians and working in partnership with stakeholders, to address the issue of global harmonization.

International data sharing and continued pharmacovigilance practices are important for monitoring and communication of the benefit / risk profile of veterinary medications. Through cooperation between governments, manufacturers and the public, communication of appropriate and prudent drug use can help maintain the effectiveness and safety of medications and of the food supply.

REFERENCES

Additional sources of information:

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