Health Products and Food Branch
Inspectorate
Graham Spry Building, 3rd Floor
250 Lanark Avenue
Address Locator # 2003D
Ottawa, Ontario
K1A 0K9

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TO: Associations

I am pleased to inform you that the "*Policy for the Importation or Sale of Active Pharmaceutical Ingredients for Veterinary Use*" has been revised due to administrative changes and is now available on the Health Products and Food Branch Inspectorate website at:

http://hc-sc.gc.ca/dhp-mps/compli-conform/index_e.html

Inquiries about this document can be addressed by e-mail at DCVIU_UVCEM@hc-sc.gc.ca.

Yours very truly,

Original signed by

Diana Dowthwaite
Director General

Health Canada
Health Products and Food Branch

OUR MANDATE:

To promote good nutrition and informed use of drugs, food, medical devices and natural health products, and to maximize the safety and efficacy of drugs, food, natural health products, medical devices, biologics and related biotechnology products in the Canadian marketplace and health system.

Health Products and Food Branch Inspectorate

Policy for the Importation or Sale of Active Pharmaceutical Ingredients for Veterinary Use

POL-0018

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August 22, 2004

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Ce document est aussi disponible en français

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1.0 Purpose

This policy describes the interpretation of the existing requirements under the *Food and Drugs Act* (the Act) and associated Regulations with respect to active pharmaceutical ingredients imported and sold in Canada for animal use. It outlines those circumstances under which the Health Products and Food Branch Inspectorate will take enforcement measures to minimize consumer health risks associated with active pharmaceutical ingredients sold in bulk for veterinary use.

2.0 Background

Some active pharmaceutical ingredients (APIs) when offered directly for administration to animals are considered to be drugs in dosage form and are issued Drug Identification Numbers (DINs). These products have been manufactured with controls offered by the Canadian drug regulatory system such as established withdrawal periods, maximum food residue limits, DIN registration, labelling standards, Good Manufacturing Practices, and Establishment Licencing.

Bulk APIs are also permitted to be sold or imported as raw materials for further modification. These products are not subject to labelling regulations, or DIN requirements and are not intended to be used as drugs in dosage form. The Health Products and Food Branch Inspectorate (HPFBI) has received numerous complaints regarding the misuse of these bulk APIs in veterinary use. These complaints include:

- the lack of Good Manufacturing Practices (GMP) with respect to these materials,
- extra-label use (e.g. the administration of clenbuterol to food-producing animals), and
- the illegal promotion, sale, and representation for use as drugs of bulk APIs to farmers, pharmacists, feed mill operators, and veterinarians.

The Enforcement Directive: *Sale of Active Pharmaceutical Ingredients as Drugs for Veterinary Use* came into effect on March 1, 1999 to set out Health Canada's position on such matters given what was taking place in the industry at that time, as bulk raw APIs were inappropriately being manufactured, sold, and represented for use as veterinary drugs in dosage form (e.g. powders, granules, and pellets for oral administration in animal feeds, powders and liquids for administration in drinking water, topical applications, or for reconstitution for injection by farmers, veterinarians, pharmacists, and feed mills). This use of APIs avoids the controls of the Canadian drug regulatory system, impacts the safety of the domestic food supply, affects the availability of high quality veterinary drugs in Canada, and may have impacts on the export of food products such as milk, meat, and eggs from this country. The *Policy for the Importation or Sale of Active Pharmaceutical Ingredients for Veterinary Use* replaced the Enforcement Directive.

It is the objective of the Health Products and Food Branch to administer the Food and Drugs Act and its Regulations, and prioritize their enforcement to minimize the health risks. These laws help promote the availability of safe and effective drug products in the Canadian market. Administering these laws will maintain a level playing field for drug manufacturers in Canada who are in compliance with the *Food and Drugs Act* and *Regulations*.

3.0 Scope

This policy applies to all bulk APIs which are destined for the Canadian market or are already being sold in Canada, and which may be sold as finished products for veterinary use.

4.0 Definitions

API	Active Pharmaceutical Ingredient
DIN	Drug Identification Number
ELDU	Extra-label drug use
GMP	Good Manufacturing Practices
HPFBI	Health Products and Food Branch Inspectorate

Active Pharmaceutical Ingredient: Active Pharmaceutical Ingredient includes any substance or mixture of substances intended to be used in the manufacture of a drug (medicinal) product and that, when used in the production of a drug, becomes an active ingredient of the drug product. Such substances are intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease or to affect the structure and the function of the body.

Extra-label drug use: “Extra-label drug use”, sometimes referred to as "off label use", is the use of a drug product in a manner that is not consistent with what is indicated on the label/package insert of any drug product approved by Health Canada.

Modification: A change in the physical or chemical characteristics of an API that will affect its composition, value, merit, presentation or quantity and will make it more suitable or safe for direct administration to animals. Some examples include relabelling, repackaging and incorporating into dosage form by an establishment licensed to fabricate drugs, or compounding pursuant to a prescription by a pharmacist, a practitioner (e.g. a veterinarian) or a person under the supervision of a practitioner.

5.0 Policy Statement

SALE AND IMPORTATION

Currently, the Health Products and Food Branch regards the sale and importation of bulk APIs in the following manner:

1. The importation and sale of bulk API's for veterinary use as drugs in dosage form must be in compliance with the relevant requirements of the *Food and Drug Regulations,* including those involving DIN, and the applicable GMP, Establishment Licensing and/or labelling provisions. Unless such importation or sale is to a licensed establishment, a pharmacist, or a practitioner and is for

modification prior to use, the APIs involved are considered to be drugs in dosage form.

- Sale of APIs to feed mills, retailers, farmers, or other end users is considered to be the sale of a drug in dosage form, requiring compliance with DIN, GMP, Establishment Licensing and labelling requirements.
- Sale of APIs to research institutions may be subject to the regulations in Part C, Division 8 regarding Investigational New Drugs and Experimental Studies Certificates.

2. The sale of API's for direct administration in an extra-label use manner to food producing animals is considered the sale of a new drug subject to the provisions of Part C Division 8 of the *Food and Drug Regulations*. In addition, Regulations C.01.610.1 and C.01.610.2 will be enforced with respect to API's and drugs in dosage form, regardless of whether the sale is made pursuant to a prescription.

3. The importation prohibition applicable to Part I, Schedule F drug substances and outlined in subsection C.01.045 (1) will be enforced, where the API could be for veterinary use, regardless of whether the drug is in finished form. This applies only to APIs which will not be subject to modification prior to use.

- All Schedule F, Part II drugs imported under the provisions of subsection C.01.045 (2) of the *Food and Drug Regulations* must comply fully with the requirements of that section. The statement "form not suitable for human use" in C.01.046 is interpreted to include only finished dosage forms, including (but not restricted to) agricultural implants, veterinary boluses and drugs mixed with animal feed, and not active pharmaceutical ingredients because they could be compounded into a form "suitable for human use".

4. Schedule F drug substances sold pursuant to a prescription have to fully comply with GMP, DIN, and labelling requirements, or have to be compounded by a pharmacist, a practitioner (e.g. a veterinarian), or a person under the supervision of a practitioner.

5. The prescribing by veterinarians and the compounding by veterinarians and/or pharmacists from products that do not have a DIN or valid DIN is to be avoided. Unless otherwise necessitated by life-threatening emergencies, veterinarians and pharmacists are encouraged to exercise the following voluntary controls when prescribing/compounding: (refer to *GUI-0030 Manufacturing and Compounding Drug Products in Canada*)

    - only drugs which have received a DIN should be used to treat food-producing animals, including the use of drug products with DINs for compounding;

    - in keeping with good medical practice, prescribing or administering drug substances for extra-label use are to be avoided in food-producing animals, especially when there are

approved therapeutic alternatives available on the Canadian market or through the Emergency Drug Release Program through the Veterinary Drugs Directorate.

COMPLIANCE AND ENFORCEMENT

Compliance and enforcement actions will be consistent with those described in POL-0001 *Compliance and Enforcement Policy,* POL-0040 *Drug Identification Number (DIN) Enforcement Policy,* POL-0004 *Good Manufacturing Practices (GMP) and Establishment Licensing Enforcement Directive* including;

- Refusal of entry or conditional entry at the border to drug products which lack evidence of DIN compliance or where the consignee is ineligible to import (e.g. Schedule F Drugs, Controlled substances or Class A Precursors).
- Recall of drug products sold without valid DIN, labelling deficiencies, lack of GMP or other violations.
- Voluntary detention, re-export, over-stickering (where the DIN has been obtained but is not shown on the label) or disposal of drug products offered for sale in violation of the Act or Regulations.
- Seizure of drug products offered for sale in violation of the Act or Regulations.
- Prosecution of firms selling drugs in violation of the Act or Regulations.
- Injunction to prevent firms from selling drugs in violation of the Act or Regulations .

6.0 Responsibilities

The implementation of this policy is the responsibility of the staff of the Health Products and Food Branch Inspectorate.

7.0 Procedures

Not applicable

8.0 Effective Date

This *Policy for the Importation or Sale of Active Pharmaceutical Ingredients for Veterinary Use* is effective as of April 1, 2007.

9.0 Associated Documents

POL-0001 *Compliance and Enforcement Policy*

GUI-0030 *Manufacturing and Compounding Drug Products in Canada*

POL-0040 *Drug Identification Number (DIN) Enforcement Policy*

POL-0004 *Good Manufacturing Practices (GMP) and Establishment Licensing Enforcement Directive*

9.1 Appendix

C.01.045. (1) Subject to subsection (2), no person other than

(a) a practitioner;

(b) a drug manufacturer;

(c) a wholesale druggist;

5-3-65 (d) a registered pharmacist; or

(e) a resident of a foreign country while a visitor in Canada,

shall import a Schedule F Drug.

4-8-93 (2) Any person may import a Schedule F Drug listed in Part II of Schedule F if the drug is imported in such form or so labelled that it could be sold by that person pursuant to section C.01.046.

C.01.046. A person may sell a drug listed or described in Part II of Schedule F to the Regulations, without having received a prescription therefore, if

(a) the drug is in a form not suitable for human use; or

17-5-01 (b) the principal display panel of both the inner label and the outer label carries, in both official languages, the statement "For Veterinary Use Only/Pour usage vétérinaire seulement" or "Veterinary Use Only/Usage vétérinaire seulement", immediately following or preceding the brand name, proper name or common name, in type size not less than one-half as large as the largest type on the label.

C.01.610.1 No person shall sell a drug for administration to animals that produce food or that are intended for consumption as food if that drug contains

16-8-94

(a) chloramphenicol or its salts or derivatives;

(b) a 5-nitrofuran compound;

20-11-97 (c) clenbuterol or its salts or derivatives;

13-8-03 (d) a 5-nitroimidazole compound; or

(e) diethylstilbestrol or other stilbene compounds.

C.01.610.2 No person shall sell an antibiotic preparation containing chloramphenicol, its salts or derivatives, for administration to animals that do not produce food and that are not intended for consumption as food unless

(a) both the inner label and outer label of the preparation carry the words "WARNING: FEDERAL LAW PROHIBITS THE ADMINISTRATION OF THIS PREPARATION TO ANIMALS THAT PRODUCE FOOD OR ANIMALS THAT ARE INTENDED FOR CONSUMPTION AS FOOD/MISE EN GARDE : EN VERTU DES LOIS FÉDÉRALES, IL EST INTERDIT D'ADMINISTRER CETTE PRÉPARATION AUX ANIMAUX QUI PRODUISENT DES ALIMENTS OU AUX ANIMAUX DESTINÉS À ÊTRE CONSOMMÉS COMME ALIMENTS";

19-9-91

(b) where the preparation is for parenteral use, the preparation contains, in the form of chloramphenicol sodium succinate, not more than one gram of chloramphenicol per vial;

(c) where the preparation is for ophthalmic use, the preparation contains not more than one per cent chloramphenicol; and

(d) where the preparation is for oral use, the preparation

(i) is in tablet or capsule form and contains not more than one gram of chloramphenicol per tablet or capsule, or

(ii) is in the form of a chloramphenicol palmitate suspension and contains not more than three grams of chloramphenicol per container.