

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 on Manufacturing and Compounding Drug Products in Canada

### POL-0051

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#### ***Disclaimer***

*This document does not constitute part of the Food and Drugs Act (Act) or the Food and Drugs Regulations (Regulations) and in the event of any inconsistency or conflict between that Act or Regulations and this document, the Act or the Regulations take precedence. This document is an administrative document that is intended to facilitate compliance by the regulated party with the Act, the Regulations and the applicable administrative policies. This document is not intended to provide legal advice regarding the interpretation of the Act or Regulations. If a regulated party has questions about their legal obligations or responsibilities under the Act or Regulations, they should seek the advice of legal counsel.*

Ce document est aussi disponible en français.

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## 1.0 Purpose

The purpose of this document is:

1. To provide background information on the compounding and manufacturing of drugs in Canada;
2. To provide a policy framework to assist in distinguishing between compounding and manufacturing activities of drug products in Canada.

## 2.0 Scope

The scope of this policy framework covers drugs for human and veterinary use. This policy applies to all scheduled drugs regulated under the *Food and Drugs Act* (i.e., Schedule C (Radiopharmaceuticals), Schedule D (Biologics), Schedule F (Prescription drugs) and Schedule G (controlled substances) as well as Over the Counter drugs). Note, however, that this policy does not apply to natural health products (NHP) regulated under the *Natural Health Products Regulations*. A separate document will be provided by the Natural Health Products Directorate for compounding NHP.

## 3.0 Background

In Canada, compounding of drugs is practised primarily by pharmacists as an integral part of their profession and is regulated by the respective regulatory authorities in each province/territory. Other healthcare professionals such as physicians, veterinarians or dentists may also be involved in compounding activities when licensed to do so by the province/territory in which they practice. Drug manufacturing, on the other hand, is regulated by Health Canada under the federal *Food and Drugs Act* and *Food and Drug Regulations*. Since the maintenance and enhancement of health and safety is a responsibility that is shared between government (federal and provincial/territorial) and industry, consumers, healthcare professionals and their respective associations, it is important that the definitions for compounding and manufacturing be clearly understood so that the respective parties can fulfil their responsibilities in a coordinated and effective way.

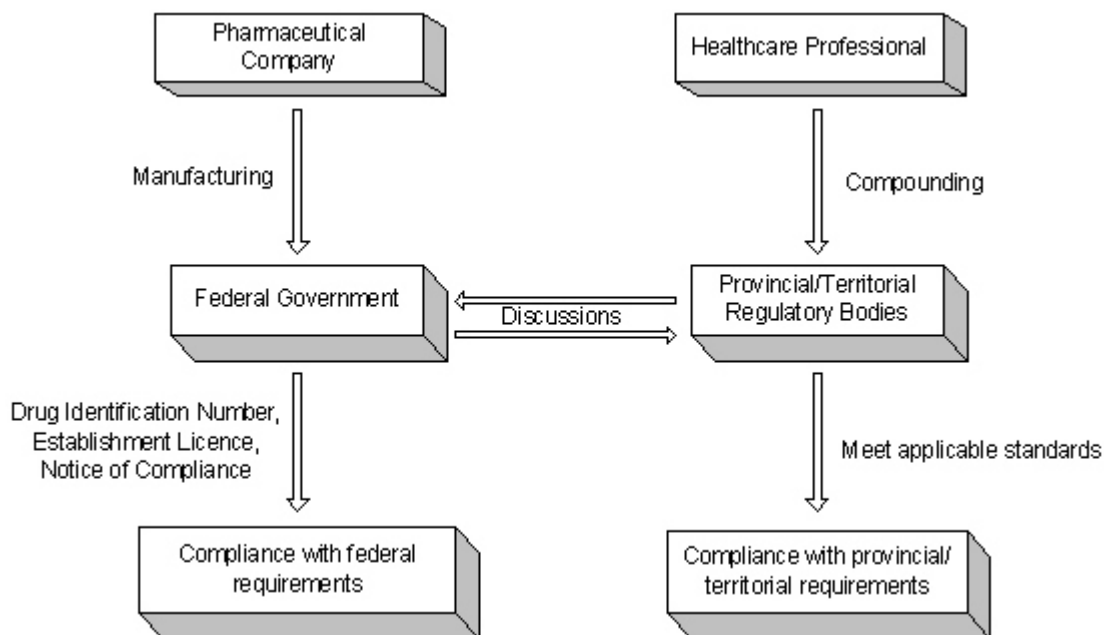
In February 1997, a multidisciplinary workshop was held on the subject of the compounding and manufacturing of drugs in Canada. The need for clarity across roles and jurisdictions, as well as concerns related to particular products, processes and service providers were among the many issues highlighted. In July 2000, the policy document entitled *Manufacturing and Compounding Drug Products in Canada* was published by Health Canada following consultation with the National Association of Pharmacy Regulatory Authorities (NAPRA) and the Canadian Society of Hospital Pharmacists (CSHP).

Since the initial workshop, the compounding market has evolved greatly. The Health Products and Food Branch Inspectorate (HPFBI) held a facilitated focus group session in April 2004 to discuss the current issues on compounding, in an attempt to better differentiate compounding from the process of manufacturing. In addition, discussions also took place on developing an uniform approach to address issues that Federal and Provincial/Territorial regulators and healthcare professionals involved in compounding are confronted with. In essence, there is a need to develop a Canada wide consistency in approach to ensure that drug compounding and drug manufacturing are each regulated by the appropriate authorities.

## 4.0 Determination of Regulatory Responsibility/Jurisdiction

The following illustration (Figure 1.0) demonstrates the process to be followed by federal regulators, provincial/territorial regulators and healthcare professionals when dealing with jurisdictional issues related to compounding and manufacturing. Adopting this process will help develop a consistent Canada wide approach ensuring that all products and activities are appropriately regulated.

Figure 1.0 - Process in addressing Manufacturing and Compounding Issues



In essence, in circumstances where an individual cannot clearly determine whether a particular activity is considered to be manufacturing or compounding, they may contact either the Health Products and Food Branch Inspectorate or the respective provincial/territorial regulatory body (see [Section 7.0 Associated Documents/Links - contact list](#)). At that point, discussions may take place between the two jurisdictions for final determination of whether an activity is considered to be compounding or manufacturing.

Note that, in situations where the provincial/territorial regulatory authority decides that an activity does not fall within its jurisdiction, the activity is likely to be manufacturing and the parties involved must follow the federally regulated drug approval process for manufactured drugs.

#### 4.1 Federal Jurisdiction

Manufacturers of drugs in dosage form must comply with the requirements of the *Food and Drugs Act* and *Food and Drug Regulations* including all associated standards and guidelines. In particular, manufactured drugs must be authorized for sale in Canada, meaning that the product authorization application received is reviewed for quality, safety and efficacy by Health Canada. In order to be sold in Canada, a drug will also require a Drug Identification Number (DIN) and/or Notice of Compliance (NOC) (Some products such as radiopharmaceuticals will not have a DIN). Furthermore all fabricators, packagers/labellers, distributors, importers, testers, and wholesalers will be required to obtain an Establishment Licence (EL) (Division 1A of *Food and Drugs Act* and *Food and Drug Regulations*), and meet the applicable sections of Division 2 relating to Good Manufacturing Practices (GMP) and comply with other relevant sections of the *Food and Drug Regulations*.

All healthcare professionals importing drug products must also comply with all applicable sections of the *Food and Drugs Act* and *Food and Drug Regulations* (C.01.005 (2) and C.01A.002(b) for importing drug products used in compounding).

All healthcare professionals compounding drug product must also comply with all relevant sections of the *Food and Drugs Act* including sections 3 - Prohibited advertising; 8 - Prohibited sales of drugs; 9 - Deception regarding drugs; and 11 - Unsanitary manufacture of drug.

## 4.2 Provincial/Territorial Jurisdiction

### *Healthcare Professionals*

For the purpose of this Policy, Healthcare Professionals are those who are licensed to practise by their respective provincial/territorial regulatory authorities. Compounding is therefore a licensed or authorized act that falls within the scope of the practice of the professions such as pharmacy and medicine/dentistry/veterinary medicine or other healthcare professionals. Healthcare professionals who are engaged in compounding must comply with applicable provincial/territorial/federal regulations and their standards for these services. The responsibility for risk arising from compounding activities is assumed by licensed healthcare professionals in the treatment and servicing of their patients/clients.

The licensing of hospital pharmacies varies from province/territory to province/territory and may also depend if drug products are supplied only within the hospital or also to outpatients and third parties. The appropriate provincial/territorial regulatory authority should be consulted for additional information.

The use of compounded drugs in food animals is discouraged and the veterinarian is solely responsible for establishing an appropriate withdrawal time when using compounded drugs. Veterinarians should be aware that Canadian global Food Animal Residue Avoidance Databank (gFARAD) will not provide advice on withdrawal period for compounded drugs.

## 5.0 Policy Statement

This policy document is intended to embody the following guiding principles (key concepts are shown in bold):

### *General Guiding Principles*

- Compounding must be a legitimate part of the practice of regulated healthcare professionals and must not be used as a means to bypass the federal drug review and approval system.
- All drug compounding and manufacturing activities performed are to be regulated and fall under either the federal or the provincial/territorial jurisdiction.
- The distinguishing between compounding and manufacturing activities is made on a case-by-case basis.

## 5.1 Compounding

Factors to be considered when assessing whether an activity is compounding:

- a) Healthcare professionals who provide compounding related services and products to patients/clients must be able to demonstrate that a **patient-healthcare professional relationship** exists.
- b) Activity is **regulated** and facility **may be inspected** by provincial/territorial regulatory authorities.
- c) It is expected that healthcare professionals who compound products will have appropriate **risk management** processes in place to manage risks associated with the compounded product and the workplace (facilities, safety etc.), in line with the standards set by their provincial/territorial regulatory bodies (for example but not limited to the toxicology, pharmacology, therapeutic value, stability, adverse reactions, labelling requirements etc. of the compounded product).
- d) A pharmacy may prepare drugs in very **limited quantities**, in anticipation of a prescription. For the purpose of this Policy, preparation involves compounding or repackaging of multiple units, not for immediate use, in a single process, by the same operator in accordance with a standardized batch preparation procedure.

- e) Compounding should only be done if there is a **therapeutic need** or **lack of product** availability and should not be done solely for economic reasons for the healthcare professionals.
- f) The compounded product must provide a **customized therapeutic solution** to improve patient care without duplicating an approved drug product.
- g) When there is a **shortage or no supply of a commercially** available product and the healthcare professional has determined a medical need for this product, the product may be compounded during the period of shortage or no supply only.
- h) Drugs should not be compounded in order to be sold to **third parties** who will in turn sell/deliver to patients outside of their defined patient-healthcare professional relationship (see definition of “sell”). Pharmacists that do not provide specific compounding services may contract this activity to another pharmacist who provides this type of specific compounding service.
- i) Compounding of **clinical trial drugs** is only permitted if this activity is authorized in the clinical trial application or experimental or investigational authorization.
- j) Product should be produced from an **authorized drug** or Active Pharmaceutical Ingredient (API) used in an authorized drug for use in Canada or listed in a **recognized Pharmacopoeia** (USP, PhEur, PhF, PhI, BP, CF, NF, Codex - *Schedule B Food and Drugs Act*.)
- k) Those engaged in sterile compounding should be knowledgeable and obtain specialized technical training in this area (The Canadian Society of Hospital Pharmacists as well as United States Pharmacopoeia (USP) have developed guidelines for the preparation of sterile preparations). Compounding of **sterile products** is only permitted in hospitals or other practice settings where carefully established standards for the operation of clean rooms and the preparation of sterile products are in place and documented, in accordance with a recognized source. The products are dispensed directly to patients or to those who administer to patients, and are operating within a demonstrated patient-healthcare professional relationship. Pharmacists may delegate some of the compounding responsibilities to pharmacy technicians if they are adequately trained in compounding sterile products or if the provincial/territorial laws authorize it.
- l) Pharmacists in hospitals providing compounding **services to other hospitals** should be within the same province, and operate under the same hospital management board (ie. inter-hospital transfer, where the hospital may be composed of several facilities at different locations).
- m) The compounded product must comply with all relevant sections of the **Food and Drugs Act** including sections 3 - Prohibited advertising; 8 - Prohibited sales of drugs; 9 - Deception regarding drugs; and 11 - Unsanitary manufacture of drug.
- n) The expiration date of the compounded product is based on known stability data. If stability data is not available, the expiration date should be short, usually limited to the duration of the prescription or use.

## 5.2 Manufacturing

An activity will be considered manufacturing in the following circumstances:

- a) Healthcare professionals who cannot demonstrate that a **patient-healthcare professional relationship** exists.
- b) Producing an identical product that is **already commercially available**, unless there is a shortage (see section on compounding).
- c) **Producing or selling** the product by a **third party**.
- d) Healthcare professionals who produce products intended for **distribution or sale outside** the demonstrated patient-healthcare professional relationship.
- e) Producing products made in such a **scale, time and frequency** to fall outside of a patient-healthcare professional relationship.
- f) Clinical trial application, experimental or investigational authorization does not specify authorization to compound **clinical trial drugs**.

- g) Producing a drug product that requires only minor modification prior to direct administration when such modification amounts to mere directions for use. Examples of such include the addition of liquid to a powder or adding a powder to animal drinking water. Compounding does not include mixing, reconstituting, or any other manipulation that is performed in accordance with the directions for use on an approved drug's labelling material (Aside added: "within the normal practice of pharmacy").
- h) **Repackaging** commercially available drugs in finished dosage form outside the normal dispensing activities within the practice of pharmacy.

General guidelines on compounding and manufacturing activities is summarized in [Appendix I](#).

For additional information, contact the appropriate provincial/territorial professional regulatory authority or Health Products and Food Branch Inspectorate in Ottawa. Refer to section [7.0 Associated Documents/Links](#) for a complete list of College of Pharmacies and Health Canada website links.

## 6.0 Definitions

### ***Active Pharmaceutical Ingredient (API):***

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 function of the body. (*ICH Q7*)

### ***Anticipation of a prescription:***

Pharmacies may prepare drugs in very limited quantities before receiving a valid prescription, provided they can document a history of receiving valid prescriptions that have been generated solely within an established patient-healthcare professional relationship, and provided further that they maintain the prescription on file as required by provincial law.

### ***Compounding:***

Health Canada considers compounding to be the following:

The combining or mixing together of two or more ingredients (of which at least one is a drug or pharmacologically active component) to create a final product in an appropriate form for dosing. It can involve raw materials or the alteration of the form and strength of commercially available products. It can include reformulation to allow for a novel drug delivery. Compounding does not include mixing, reconstituting, or any other manipulation that is performed in accordance with the directions for use on an approved drug's labelling material (Aside added: "within the normal practice of pharmacy").

For other definitions of compounding, see Section [7.0 Associated Documents/Links](#) (USP, NAPRA, QCP, NSCP).

### ***Customized Medication:***

A formulation resulting from the combination of drugs or, APIs and/or non-medicinal ingredients that meets the patient's or animal's specific therapeutic needs.

### ***Patient-Healthcare Professional Relationship:***

A relationship that can be demonstrated to exist between a patient and a regulated healthcare professional in which a professional service is provided. When the relationship involves an animal, a valid veterinarian-client-patient relationship (VCPR) is required.

***Healthcare Professional:***

A person lawfully entitled under the laws of a province or a territory to provide health services in the place in which the services are provided by that person including a pharmacist, dentist, medical practitioner or a veterinarian.

***Patient:***

An individual or animal with unique requirements receiving medical treatment distinct from a group.

***Pharmacist:***

An individual who (a) is registered or otherwise authorized under the laws of a province or territory to practise pharmacy; and (b) is practising pharmacy in that province.

***Prescription:***

An order given by a practitioner directing that a stated amount of any drug or mixture of drugs specified therein be dispensed for the person named in the order (*Food and Drug Regulations C.01.001*).

***Repackaging:***

Subsiding or breaking up a manufacturer's original package of a drug for the purpose of dividing and assembling the drug in larger or smaller quantities for redistribution or sale by retail.

***Sell:***

Includes offer for sale, expose for sale, have in possession for sale and distribute, whether or not the distribution is made for consideration. (*Food and Drugs Act*)

***Third Party:***

Any individual, organization, or company outside of a patient-healthcare professional or valid veterinarian-client-patient relationship.

***Valid Veterinarian-Client-Patient Relationship (VCP or VCPR):***

See Patient-Healthcare Professional Relationship

A valid VCPR exists when these conditions apply:

- The client (owner or owner's agent of the animal[s]) has given the responsibility of medical care to the veterinarian and has agreed to follow the instructions of the veterinarian, and;
- the veterinarian has assumed the responsibility from the client for making clinical judgement regarding the health of the animal(s), the need for medical treatment, and for ensuring the provision of ongoing medical care for the animal(s);
- the veterinarian has sufficient knowledge of the health status of the animal(s) and the care received or to be received. The knowledge has been obtained through a recent examination of the animal(s) and the premises where they are (it is) kept or through a history of medically appropriate and timely examinations and interventions, and;
- the veterinarian is readily available, or has made the necessary arrangements with another veterinarian, for ongoing medical care of adverse reactions or therapy failure.

***Withdrawal Period:***

The length of time between the last administration of a drug to an animal and the time when tissues or products collected from the treated animal for consumption as food contain a level of residue of the drug that would not likely cause injury to human health. (*Food and Drug Regulations C.01.001*)



## 7.0 Associated Documents/Links

*Guidelines for Bulk Compounding of Products in Hospitals*, Canadian Society of Hospital Pharmacists, Ottawa, Ontario 1992.

*Guidelines for Preparation of Sterile Products in Pharmacies*, Canadian Society of Hospital Pharmacists, Ottawa, Ontario 1996.

*Guidelines for Repackaging Products in Healthcare Facilities*, Canadian Society of Hospital Pharmacists, Ottawa, Ontario 1998.

*Guidelines For The Legitimate Use Of Compounded Drugs in Veterinary Practice*, Canadian Veterinary Medical Association, 2005

*Guidelines to Pharmacy Compounding (Draft)*, National Association of Pharmacy Regulatory Authorities (NAPRA), Ottawa, Ontario 2005

*Model Standards of Practice for Canadian Pharmacists*, National Association of Pharmacy Regulatory Authorities (NAPRA), Ottawa, Ontario 2003.

*National Association of Boards of Pharmacy Good Compounding Practices Applicable to State Licensed Pharmacies*. National Association of Boards of Pharmacy. Park Ridge, IL, 2001; 151.

USP Chapter <795> Pharmaceutical Compounding: Nonsterile Preparations

USP Chapter <797> Pharmaceutical Compounding: Sterile Preparations

Some of the following hyperlinks are to sites of organizations or other entities that are not subject to the [Official Language Act](#). The material found there is therefore in the language(s) used by the sites in question

### Website addresses:

#### College of Pharmacies

British Columbia	<a href="#">College of Pharmacists of British Columbia</a>
Alberta	<a href="#">Alberta college of pharmacists</a>
Saskatchewan	<a href="#">Saskatchewan College of Pharmacists</a>
Manitoba	<a href="#">Manitoba Pharmaceutical Association</a>
Ontario	<a href="#">Ontario College of Pharmacists</a>
Quebec	<a href="#">Ordre des pharmaciens du Québec</a>
New Brunswick	<a href="#">New Brunswick Pharmaceutical Society</a>
Nova Scotia	<a href="#">Nova Scotia College of Pharmacists</a>
Newfoundland	<a href="#">Newfoundland &amp; Labrador Pharmacy Board</a>
Prince Edward Island	<a href="#">Prince Edward Island Pharmacy Board</a>
Yukon	<a href="#">Yukon Community Services</a>
Northwest Territories	<a href="#">Northwest Territories Department of Health and Social Services</a>

#### Health Canada

DIN Applications:	<a href="#">Guideline on Preparation of DIN Submissions</a>
Drug Establishment Licences:	<a href="#">Drug Establishment Licences</a>
Drug Submissions:	<a href="#">Guidance on Drug Establishment Licences (GUIDE-0002)</a>

EDR: [Veterinary Drugs - Emergency Drug Release \(EDR\)](#)  
Good Manufacturing Practices: [Good Manufacturing Practices - Guidance documents](#)  
HPFBI: [Health Products and Food Branch Inspectorate - Compliance and Enforcement](#)  
SAP: [Special Access to Drugs and Health Products](#)

**Associations**

ASHP: [American Society of Health-System Pharmacists](#)  
CSHP: [Canadian Society of Hospitals Pharmacists](#)  
NAPRA: [National Association of Pharmacy Regulatory Authorities](#)

**8.0 Authors**

This Policy Framework was developed by the Health Products and Food Branch Inspectorate in collaboration with other Health Products and Food Branch directorates and members of the April 2004 focus group session.

**Appendix I**  
**General Guideline on Compounding and Manufacturing Activities**

<b>Compounding</b>		<b>Manufacturing</b>
Yes	1) Is there a demonstrated patient-healthcare professional relationship?	No
No	2) Is there third party reselling of the product outside of the patient-healthcare professional relationship?	Yes
Yes	3) Is the activity regulated, and facility possibly inspected, by the province/territory?	No
Yes	4) If producing product in anticipation of a prescription, is the amount produced consistent with the history of prescriptions received?	No
No	5) Is there an inordinate amount of product produced or on a regular basis?	Yes
No	6) Is an identical product (e.g. dosage form, strength, formulation) commercially available?	Yes
No	7) Is the product and/or compounding service promoted or advertised to the general public rather than strictly to healthcare professionals?	Yes
No	8) Does the drug product require only minor modification prior to direct administration when such modification amounts to mere directions for use?	Yes