Health Canada Santé Canada

Draft guidance document: Labelling of pharmaceutical drugs for human use

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Canada

Foreword

Guidance documents are meant to provide assistance to industry and healthcare professionals on **how** to comply with governing statutes and regulations. Guidance documents also provide assistance to staff on how Health Canada mandates and objectives should be implemented in a manner that is fair, consistent and effective.

Guidance documents are administrative instruments not having force of law and, as such, allow for flexibility in approach. Alternate approaches to the principles and practices described in this document ***may be*** acceptable provided they are supported by adequate justification. Alternate approaches should be discussed in advance with the relevant program area to avoid the possible finding that applicable statutory or regulatory requirements have not been met.

As a corollary to the above, it is equally important to note that Health Canada reserves the right to request information or material, or define conditions not specifically described in this document, to allow the Department to adequately assess the safety, efficacy or quality of a therapeutic product. Health Canada is committed to ensuring that such requests are justifiable and that decisions are clearly documented.

This document should be read in conjunction with the accompanying notice and the relevant sections of other applicable guidance documents.

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1. Introduction

1.1 Policy Objectives

It is Health Canada's policy that labelling of pharmaceutical drug products for human use:

1. complies with the labelling requirements pursuant to sections 3, 9, and 10 of the *Food and Drugs Act* (the *Act*),as well as related provisions of the *Food and Drug Regulations* (the *Regulations*), the *Controlled Drugs and Substances Act*, and its related *Regulations* including the *Narcotic Control Regulations*, Parts G and J of the *Food and Drug Regulations* and the *Benzodiazepines and Other Targeted Substances Regulations*;
2. is consistent with the Health Canada guidance documents and policies that apply to pharmaceutical drug products for human use; and
3. supports the safe and effective use of drug products by healthcare professionals, patients, and consumers.

1.2 Scope and Application

This guidance document is applicable to pharmaceutical drug products for human use. It is **not** applicable to disinfectants, drug products for veterinary use, drug products used in clinical trials, drug products regulated solely as natural health products subject to the provisions of the *Natural Health Products Regulations*, and radiopharmaceuticals and biological drug products as listed in Schedules C and D of the *Food and Drugs Act*. This guidance document contains:

- excerpts from the *Food and Drugs Act* and *Food and Drug Regulations*, and related Acts and Regulations;
- definitions of terms; and
- current interpretations of labelling requirements based on precedents, advisory opinions, and precedent drug product decisions.

The examples provided in this guidance are for illustrative purposes only and do not represent actual drug products.

1.3 Background

Labelling of Pharmaceutical Drugs for Human Use replaces the Health Canada guidance document *Labelling of Drugs for Human Use*. This guidance document came into effect in 1989, was subsequently revised in 1991, and has since been removed from circulation by Health Canada because much of its content was deemed to be out-of-date.

The purpose of this document is to provide guidance to sponsors to facilitate compliance with the labelling requirements pursuant to sections 3, 9, and 10 of the *Food and Drugs Act* as well as related provisions of the *Food and Drug Regulations*, the *Controlled Drugs and Substances Act*, and its related *Regulations* including the *Narcotic Control Regulations*, Parts G and J of the *Food and Drug Regulations* and the *Benzodiazepines and Other Targeted Substances Regulations*. This guidance should be used in conjunction with any other relevant Health Canada guidelines, policies and technical documents. Adherence to this guidance is expected to support the safe and effective use of drugs by health care professionals, patients and consumers.

The guidance document reflects comments from the draft posted to the Health Canada website on July 7, 2010 with a 120 day external stakeholder comment period ending November 7, 2010. There was substantial

input from industry and industry associations representing innovator and generic companies as well as Health Canada employees. All stakeholder comments were considered in the finalization of this guidance document.

This document also reflects revisions made as a result of the *Regulations Amending Certain Regulations Concerning Prescription Drugs* (Repeal of Schedule F to the *Food and Drug Regulations*) which provided for the repeal of Schedule F and incorporation by reference of a list of prescription drugs. This regulatory amendment came into effect on December 19, 2013. In addition, on July 2, 2014, Health Canada published in Canada Gazette, Part II, other amendments to the *Food and Drug Regulations*. The *Regulations Amending the Food and Drug Regulations (Labelling, Packaging and Brand Names of Drugs for Human Use)* introduced targeted amendments to emphasize the importance of plain language labelling. These regulatory amendments come came into force on June 13, 2015 for prescription products and products which are administered or obtained through a health professional. This guidance document reflects the new requirements set out in the above amendments as well as comments from stakeholders received during the consultation period for the Plain Language Labelling amendments, which took place from July to September 2014.

2. General Labelling Requirements

The labelling of drug products is governed by sections 3, 9, and 10 of the *Act* and by sections contained in Parts A, C, D, G, and J of the *Regulations*. Part A is more general and refers to the labelling of food and drug products, whereas parts C, D, G, and J refer to drug products only.

Section 9 of the *Act* states that:

1. No person shall label, package, treat, process, sell or advertise any drug in a manner that is false, misleading or deceptive or is likely to create an erroneous impression regarding its character, value, quantity, composition, merit or safety.
2. A drug that is not labelled or packaged as required by, or is labelled or packaged contrary to, the *Regulations* shall be deemed to be labelled or packaged contrary to subsection (1).

Section 3 of the *Act* states that:

1. No person shall advertise any food, drug, cosmetic or device to the general public as a treatment, preventative or cure for any of the diseases, disorders or abnormal physical states referred to in Schedule A.
2. No person shall sell any food, drug, cosmetic or device
    a. that is represented by label, or
    b. that the person advertises to the general public as a treatment, preventative or cure for any of the diseases, disorders or abnormal physical states referred to in Schedule A.

For exceptions to section 3(1) of the *Act,* please refer to section 2.7, "Schedule A Claims," of this guidance. Sponsors should consult the *Regulations* for specific labelling requirements for specific drug products, as this information is not part of this guidance document. For more information on section 10 of the *Act,* please refer to section 3.4.3 of this guidance.

2.1 Placement of Information

Specific requirements of the *Food and Drug Regulations* for the placement of information on labels are summarized below. Health Canada's interpretation of these requirements is further detailed in Section 3, "Label Information," of this guidance document.

2.1.1 Principal Display Panel

The principal display panel (that is (i.e.) main panel) is the main product display surface visible to the user under normal or customary conditions of display or use. Pursuant to sections C.01.004 and C.01.005 of the *Regulations*, the principal display panel of an inner and outer label must normally show[1] the following information:

- The brand name of the drug product or if no brand name exists the proper or common name of the drug product, if applicable;
- The proper or common name of the drug product, if applicable;
- The notation "sterile (stérile)," if required by the *Regulations*;
- The symbol corresponding to the appropriate schedule or to a drug containing an ingredient listed in the Prescription Drug List (if applicable); and
- The Drug Identification Number (DIN).

2.1.2 Any Panel

Pursuant to section C.01.004 of the *Regulations*, the following information must normally[2] be displayed on any panel of the inner and outer labels:

- The name and address of the manufacturer/sponsor and of the distributor if the manufacturer/sponsor is not Canadian;
- The lot number;
- The expiration date;
- Adequate directions for use of the drug product; and
- A quantitative list of the medicinal ingredients of the drug product.

The following information is to be displayed on any panel of the outer label:

- The net amount of the drug product in the container in terms of weight, measure or number (for example (e.g.) number of tablets); and
- A quantitative list of all preservatives in parenteral preparations and of all mercurial preservatives in any drug product containing mercury or a salt or derivative thereof as a preservative.

For prescription pharmaceutical products and those products administered or obtained through a health professional, section C.01.004.01(1) requires that

- Labels of drugs for human use in dosage form include information for a contact person in Canada (e.g., telephone number, email address, website address, postal address or other information that allows communication) and
- A statement that harms associated with the use of the drug can be reported to that person.

Examples of acceptable statements include: "For questions or to report problems, please contact..." or "Questions or concerns", followed by the contact information. The name of the contact person does not need to be listed.

2.2 Official Languages

The *Regulations* state that:

The adequate directions for use required to be shown on the inner and outer labels of a drug pursuant to section C.01.004 (1) (*c*) (iii) shall be in both the French and English languages if the drug is available for sale without a prescription in an open self-selection area. (section A.01.015 (2))

An "open self-selection area" is a retail area where a drug product is freely available for selection and purchase by the general public. Therefore, prescription drug products, drug products available in hospitals and clinics only, or drug products for professional use only do not require bilingual labelling. The manufacturer/sponsor can label these drug products in the customer's choice of language.

Note that some provincial regulatory requirements may go beyond existing federal *Regulations* and may specify further labelling language requirements.

There is no objection to the use of additional languages in product labelling (e.g., inserts), at the discretion of the sponsor, provided this does not obscure the readability of the label in either or both official languages, English and French.

Note: As of June 13, 2015, new requirements for the filing of mock-ups of labels and packages apply to prescription products and those products administered or obtained through a health professional. Additionally, the requirement to submit final labels at the time of market notification is repealed for these products as of this date. As a result, Health Canada expects that sponsors will file bilingual mock-ups of the labels and packaging at the time of submission[3] for prescription products and those administered or obtained

through a health professional as of June 13, 2015. For more information on this provision, please see section 2.10 of this guidance.

2.3 Legibility

The *Regulations* are flexible regarding type size. However the *Regulations* state:

All information required to appear on a label of a food or drug shall be:

a. clearly and prominently displayed on the label; and
b. readily discernible to the purchaser or consumer under the customary conditions of purchase and use (section A.01.016).

For prescription products and those products administered or obtained through a health professional, as of June 13, 2015, section A.01.017 sets out new requirements:

Every label of a drug for human use in dosage form shall meet the following conditions:

a. the information that is required by these Regulations to appear on the label shall be
    i. prominently displayed,
    ii. readily discernible to the purchaser or consumer under the customary conditions of purchase and use, and
    iii. expressed in plain language; and
b. the format of the label, including the manner in which its text and any graphics are displayed on it, shall not impede comprehension of the information referred to in paragraph (*a*).

Sponsors should consider the colour, contrast, position, and spacing of the information when complying with the above general requirement. The format of the label including the manner in which all of its text and any graphics are displayed on it, shall not impede comprehension of the information referred to in (a) above. Health Canada recommends a font size of ten points for the consumer information/patient medication information and package insert text and a minimum of nine points for inner and outer labels and tables for the labelling of the consumer information/patient medication information and package inserts, preferably all labelling in Sans Serif type font, to avoid any problems in legibility. It is recognized that under some conditions such as font type, colour, contrast, spacing and other factors, smaller font size may be legible, but it is the manufacturer's/sponsor's responsibility to ensure that this is readable to most people with normal vision. For further information, concerning the consumer information/patient medication information format, content and readability refer to the *Guidance to Industry: Product Monograph*.

2.4 Abbreviations

Generally the proper or common names of the drug product and any ingredient in the drug product should **not** be abbreviated.

The names of pharmacopoeiamay be abbreviated as indicated in Schedule B of the *Act*. Units of weight, volume, or potency may be abbreviated according to the *Weights and Measures Act* or where that abbreviation is in common use and considered to be understood by the healthcare professional or consumer. Standard units of measure and abbreviations (e.g., ounces, oz.) may be included on the label provided that the metric units are also present. Recognized abbreviations for microgram are "µg" and "mcg." The symbol "µg" conforms to the International System of Units and is often used in scientific literature. However, regarding drug product labelling, Health Canada recommends that the abbreviation "mcg" be used. This use of "µg" may be difficult to see in some print and size formats and might be misread as the prefix "mg.".

Abbreviations used exclusively to describe routes of administration (e.g., "i.v." "For intravenous injection") or other product attributes are generally discouraged in consumer labelling and most product monographs,

prescribing information documents and prescription labels. Abbreviations should be explained in full at least once if used elsewhere in the labelling. Only labels affixed to small containers (e.g., vials, ampoules) may contain only an abbreviation (e.g., i.v.) provided that the outer labelling (e.g., carton) indicates the term in full.

For further information regarding the use of abbreviations in drug product labelling, see the resources listed in Appendix C.

2.5 Reference to the Act and Regulations

The *Regulations* state that:

> No reference, direct or indirect, to the *Act* or to these *Regulations* shall be made upon any label or in any advertisement for a drug unless such reference is a specific requirement of the *Act* or these *Regulations* (section C.01.007)

Labels that may be considered in violation of section C.01.007 are those that make any mention of Health Canada or a component of Health Canada. This includes but is not limited to the following phrases and symbols:

- Health Canada approved, Health Products and Food Branch (HPFB) approved, Therapeutic Products Directorate (TPD) approved;
- Registered (endorsed, promoted, acceptable or recommended) by Health Canada, (HPFB, TPD, or any other acronym commonly associated with Health Canada); or
- Use of the Health Canada logo.

2.6 Voluntary Industry Guidelines

This guidance document provides an interpretation of the minimum label requirements for pharmaceutical drug products. Numerous third party guidance documents exist, many by independent professional associations or public interest groups, which provide further optional guidance for labelling. Additional product labelling, standardized formatting, or other considerations suggested by these documents are acceptable provided they do not conflict with regulatory requirements. See Appendix C for other sources of guidance for labelling.

2.7 Schedule A Claims

Section 3 of the *Act* prohibits the labelling and advertising of a drug product to the general public, as a treatment, preventative, or cure for the diseases, disorders, or abnormal physical states, including synonymous names, listed in Schedule A of the *Act*. However, there are three cases where Schedule A diseases can be mentioned in labelling:

1. Pursuant to section C.01.010 of the Regulations, where mention of the condition is necessary to provide adequate directions for the safe use of a parenteral drug product or a drug containing an ingredient listed in the Prescription Drug List (i.e. prescription drug);
2. When such conditions are mentioned as part of precautions or contraindications; and
3. Under sections A.01.066 to A.01.068 of the *Regulations*, non-prescription drug products can be labelled with a preventive claim related to a disease listed in Schedule A. Refer to the Health Canada guidance document, *Schedule A and Section 3 to the Food and Drugs Act*, effective October 26, 2011, for further information. Note that pre- market authorization is required for these preventative claims as outlined in this guidance.

2.8 Novel Label Formats

Novel label formats such as peel-back, accordion labels, tags, collar labels, rotating sleeve bottle labels, and labels on the inside of cartons, bottom of containers, or in any other unusual locations may be acceptable provided that:

1. gaining access to these labels does not destroy or harm the integrity of the labelling (i.e. it can be read after opening);
2. consumers and patients are alerted to the location of the labelling information; and
3. placement of information does not otherwise contravene the *Regulations*.

Information required by the *Regulations* (C.01.004) to be on the inner and outer label (e.g., brand name, proper or common name, potency, DIN, manufacturer/sponsor, and indication, class or purpose) must be clearly visible. Also, it should be read without the need to further manipulate a novel label format (see section 2.1.1 and section 2.1.2). In other words, obtaining this critical information does not require the opening or destruction of any outer label, the opening of an accordion label, the opening of a panel, or the opening of the carton itself to gain access to information on the inside.

Note: For prescription products and those products administered or obtained through a health professional, as of June 13, 2015, section C.01.004.01(1) sets out new requirements:

C.01.004.01 (1) Every label of a drug for human use in dosage form shall display the following:

a. a telephone number, email address, website address, postal address or any other information that enables communication with a contact person in Canada; and
b. a statement to the effect that any injury to a person's health that is suspected of being associated with the use of the drug may be reported to the contact person.

(2) Subsection (1) does not apply to the labels of a drug that is listed in Schedule C or D to the Act and that is in dosage form.

For examples of acceptable statements please see section 2.1.2 of this *Guidance.*

These novel label formats should be clearly identified and explained in the drug product submission.

2.9 Bar Codes

Bar codes may be used on a drug product label for appropriate purposes (retail inventory, tracking, confirmation of identity, or potency) provided that:

1. all regulatory requirements concerning the label have been met and the bar code information does not change the terms of market authorization for the product; and
2. the bar code does not obscure or displace the required and approved information on the label, especially on small product labels.

See Appendix C of this guidance for further information.

2.10 Final Labels

Final labels (in English and/or French) should accurately represent the marketed labels, including final complete text, text layout, font size, and text order as well as any other symbols, pictures, notations, diagrams, graphs, pictorials, logos, and visible marks which could be considered therapeutic label content (e.g., pictures of electroencephalography or [EEG] recordings). Such marks or label content may state or imply certain therapeutic benefits or attributes that are inconsistent with the terms of market authorization for the drug product and may be in contravention of the *Act* and *Regulations*.

All proposed photographs or equivalent should be submitted, as a description of the image is not considered sufficient. There have been photographs added to drug product labelling following review, which have been found to be misleading and in violation of the *Act*. Photographs or equivalent, other than those intended to assist in directions for use or product safety are discouraged, due to potential to mislead the patient/consumer (e.g., lifestyle pictures for drug products intended for serious conditions).

Material considered artwork (e.g., colour, design, abstract, and flashes) as well as the design, contrast and texture of the paper cannot imply misleading therapeutic attributes of the product. These factors should not impact the readability of the labels. Manufacturers/sponsors are responsible for ensuring that final labels are clearly written, legible and consistent with the approved market authorization.

Prescription Products and Products Administered or Obtained Through a Health Professional
As of June 13, 2015, and pursuant to C.01.014.1(2)(m.1) and C.08.002(2)(j.1), bilingual mock-ups of the final labels (including mock-ups of the inner and outer label and package), the package insert and the Product Monograph are required at the time of submission. Note that for these products only, as of June 13, 2015, the regulatory requirement in C.01.014.3 to submit final labels after the drug is available for sale, is repealed.

Products Other than Prescription and Those Administered or Obtained Through a Health Professional
The written text of proposed labels or in the case of a new drug, drafts of every label, are required at the time of submission in accordance with sections C.01.014.1 (2)(m) and C.08.002(2)(j). Although not required, sponsors may provide mock-ups of the final labels at the time of submission. Note that final labels must be submitted at the time of market notification as per section C.01.014.3.

3. Label Information

The definition of label in the *Act* (see Appendix A: Definitions) is interpreted to include labels affixed to the container or packaging of the drug, any separate package inserts, product monographs, prescribing information, fact sheets, consumer information/patient medication information (i.e., patient leaflets), patient diaries, or other material containing information specific to the drug product. These separate package labels generated by the manufacturer/sponsor may be included in the packaging or supplied to the consumer at the time of dispensing.

Health Canada generally considers labels affixed by pharmacists to fall under the practice of pharmacy and therefore be regulated by the provinces and territories. Nevertheless, regulatory provisions exist in the *Food and Drug Regulations* that are directed at pharmacy labels (e.g. C.01.005(2)) indicating that the definition of 'label' in the *Food and Drugs Act* is considered to encompass these labels.

3.1 Labelling Versus Other Product Information

Certain drug product information, such as advertising, promotional material and general disease information are generally not considered to be drug product labelling and should not appear in the labelling and packaging material. Differentiating this material from labelling is often difficult.

Certain manufacturer/sponsor generated product information distributed to patients and consumers at the time of dispensing may or may not be considered labelling, as follows:

Not likely to be considered labelling:

- Information regarding a disease that provides a comprehensive, balanced, and complete discussion of treatment options and does not emphasize a particular drug product or therapy is not considered labelling. This material should not be included in the product labelling.

Possibly considered labelling, depending on use:

- Meal plans (e.g., an aid for those taking cholesterol-lowering drug products);
- Patient diaries to record diet, exercise, weight loss; and
- Lifestyle advice in support of a drug therapy (e.g., auxiliary methods to cope with a smoking cessation regimen).

Likely unacceptable material that is not suitable in product labelling if distributed to patients includes: advertising or promotional material.

In addition, drug product information in the form of scientific papers, symposia, review articles, reports, or summaries produced by bodies independent of the manufacturer/sponsor (e.g., scientists, researchers, healthcare professionals, patient interest groups, healthcare professional associations, public bodies, and governments), should not be included as the information may not be balanced.

3.1.1 Distribution at the Time of Dispensing

Manufacturer/sponsor generated labelling, distributed at the time of dispensing or purchase, containing information that improves patient compliance or contributes to the effective and safe use of the drug product should be submitted and subject to a Health Canada review.

If the above material mentions the brand name, product name, or several products to be used together (e.g., statin and a diuretic), then it is considered labelling and subject to a Health Canada review. In other cases, the context and use of this information must be examined on an individual basis to determine whether the

material is labelling or other information, such as advertising or general disease information which is not considered appropriate.

Labelling material containing non-drug product information (e.g., general disease information), should be submitted to Health Canada for review. This information would be reviewed with respect to the *Act* and *Regulations* to determine whether it is appropriate to include this information in the drug product package. Much of this auxiliary information has been refused as it may be irrelevant, confusing, or misleading, as the consumer may feel this information and directions it may contain are necessary for treatment, when this is not the case. Part III of the Product Monograph, Consumer Information/ Patient Medication Information, is considered to be the complete and sufficient product information.

Any other auxiliary product information that may have been endorsed by third parties, such as the Pharmaceutical Advertising Advisory Board (PAAB) should **not** be included in, attached to or distributed with the drug product package at the time of dispensing of the product. Healthcare professionals (e.g., doctors) may distribute this auxiliary information (e.g., PAAB reviewed material) independently of the drug product package information, at their own discretion.

3.1.2 Distribution after Dispensing and Purchase

Any auxiliary labelling material that exceeds the limits of market authorization for the drug product, such as representing new claims or indications, should be submitted to Health Canada for review.

Auxiliary material which is distributed after the drug product is dispensed does not require a review by Health Canada if it is consistent with the approved product labelling. Manufacturers/sponsors should continue to voluntarily forward this material for review to an independent, self-regulated, industry body (e.g., the Pharmaceutical Advertising Advisory Board), which voluntarily reviews post-market, product-specific material.

Additional information is provided in the Health Canada policy document, *The Distinction between Advertising and Other Activities* listed in Appendix B.

3.2 Inner Label

In Section A.01.010 of the *Regulations*, the inner label is the label affixed to an immediate container of the drug product.

3.3 Outer Label

In Section A.01.010 of the *Regulations*, the outer label includes any label affixed to the drug product packaging, such as a pouch, card, accordion label, or other construct. There may be more than one outer label in a multiple packaging scheme (e.g., a vial packaged in a pouch, pouch enclosed in a carton, several cartons enclosed in a larger carton). Where a package of a drug product has only one label, that label must carry all the information required on the inner and outer labels (section C.01.006).

A shipping carton, unless it is also the immediate container, or the outside of the package unit distributed to the consumer or healthcare professional, is not subject to the labelling provisions of Part C, Division 1, of the *Regulations*. However, manufacturers/sponsors should note that shipping cartons must be labelled to ensure compliance with the Good Manufacturing Practices (GMP) requirements of Part C, Division 2, of the *Regulations* and associated guidance documents (see Appendix B). Health Canada recommends that manufacturers/sponsors label the shipping carton with sufficient information to enable product identification (e.g., brand name, common or proper name, strength, and manufacturer's/sponsor's name, and Drug Identification Number).

3.4 Main Panel

This subsection provides detailed information to be included on the main panel of an inner and/or outer label.

3.4.1 Brand Name

The brand name is the name assigned by the manufacturer/sponsor and approved by Health Canada in connection with a drug product at the time of market authorization. In the case of a new drug, the brand name is the name that appears on the Notice of Compliance. For Division 1 drugs[4], the brand name is the name appearing on the Drug Notification Form issued for the drug product and signed by the manufacturer/sponsor. The brand name must be consistent on all labelling. Note that a brand name is not required if manufacturer/sponsor chooses to use a common or proper name instead of a brand name as the drug product name (e.g., Acetylsalicylic Acid Tablets).

Any alteration of the brand name of a new drug from the original market authorization issued by Health Canada requires the submission and approval of a New Drug Submission (NDS) or Administrative New Drug Submission pursuant to section C.08.003 (2) (*b*) of the *Regulations*. If the drug product received market authorization as a Division 1 drug1, a new application for a Drug Identification Number (DIN) should be submitted and prior approval is required before the new name can be used. For further information, see the Health Canada policy document, *Changes in Manufacturer's Name and/or Product Name*.

The Health Canada approved brand name must be presented in a continuous, uninterrupted fashion on the label, and be clearly evident to consumers and healthcare professionals.

3.4.2 Proper or Common Name

Pursuant to section C.01.004 (1) (*a*) of the *Regulations,* when a drug product has a proper or a common name, this name must appear on the main panel of the inner and outer labels. Proper or common names should not be abbreviated. In the case of official drugs labelled with a brand name, the lettering of the proper name must be in type not less than half the size of the brand name and must immediately precede or follow the brand name.

For drug products labelled without a brand name, the proper or common name of the drug product must be shown on the main panel.

3.4.2.1 Proper Name

The proper name for an **ingredient** is considered to be the name:

1. assigned to that ingredient in section C.01.002 of the *Regulations*;
2. that appears in boldface type in other sections of the *Regulations*; or
3. assigned to the ingredient in the titles of monographs of Schedule B publications.

Where a proper name for an ingredient appears both in the *Regulations* and in one or more Schedule B publications, the name appearing in the *Regulations* takes precedence.

The proper name for a drug product includes the dosage form and is the name assigned to that final product in one of the Schedule B publications (e.g., Azithromycin Capsules).

Official synonyms for proper names listed in some Schedule B publications may be used instead of the title of the monograph, except where the synonyms are abbreviations or are in a language other than French or English. For example, the *British Pharmacopoeia* (BP)lists acceptable synonyms in Appendix XXI and these may be used in place of the non-abbreviated name. This practice is not allowed in the *United States Pharmacopoeia* (USP).

Some illustrative examples of proper names for ingredients versus products in final dosage form include the following:

- Proper name of ingredient: Acetaminophen;
- Proper name of drug product in final dosage form:Acetaminophen Capsules;
- Proper name of a drug product combination: Acetaminophen and Pseudoephedrine Hydrochloride Tablets.

If the sponsor would like to include the standard of manufacture (e.g., *United States Pharmacopoeia [USP], British Pharmacopoeia (BP), European Pharmacopoeia [Ph.Eur.]*), this should be shown in close proximity (see Appendix A, Definitions) to the proper name (e.g., Acetaminophen Capsules USP, Acetaminophen and Pseudoephedrine Capsules USP).

Note: In the USP the term "aspirin[5]" appears as a proper name for an ingredient and as a proper name for a drug product in final dosage form (e.g., Aspirin Tablets). However, in Canada, Acetylsalicylic Acid is the prescribed name (i.e. proper name) for this ingredient as outlined in section C.01.002 of the *Regulations*. In this case, the name in the *Regulations* takes precedence and if it meets USP requirements, the final product is labelled in Canada as Acetylsalicylic Acid Tablets USP.

3.4.2.2 Common Name

A common name is used in the case where there is no proper name. The common name of a drug substance is a name chosen by a respected body responsible for drug nomenclature, often with international recognition (e.g., International Non-proprietary Name [INN], United States Adopted Name [USAN], and British Approved Name [BAN]). The common name of a drug product consists of the common name of the drug substance and the dosage form.

For drug substances in the form of a salt where there is no existing common name for the drug product, the naming conventions outlined in the *USP Nomenclature Policy (See Appendix C)* are used to determine the common name of the drug product:

- Where the strength is expressed in terms of the salt, the same salt is used as the common name for the drug product.
- Where the strength is expressed in the terms of a free acid or base, the same acid or base is used in the common name of the drug product, and the name of the complete salt is also shown near this common name, on the main panel of the label. Example (where the strength is expressed in terms of the base): Brand X Antibacterial Agent, Moxifloxacin Tablets 400 milligram (mg) (as moxifloxacin hydrochloride).

As the *Regulations* require that the proper or common names of the drug products must appear on the main panel of the label, the *USP Nomenclature Policy* and the additional provision above, ensure that the complete salt is also shown on the main panel. These provisions ensure that the product identity is clear and prevents inappropriate substitutions of one salt for another, where differences in the pharmaceutical or pharmacological properties may cause adverse effects.

With respect to *different solvated forms (e.g., including hydrates),* the complete common name, including the solvated form, should be stated somewhere on the label (i.e. it does not have to appear on the main panel, as per the salts).

3.4.2.3 Pharmaceutical Form

Where a proper or common name for a drug product does not exist (e.g., for a multiple ingredient product), the pharmaceutical form should be shown on the main panel of the inner and outer label.

3.4.3 Standard of Manufacture

This section refers to the *standard* to which a drug product is manufactured and represented. The term standard can be applied to a drug product or to an ingredient.

Where a standard prescribed by the *Regulations* exists (see Section 3.4.3.1, "Prescribed Standard") and it applies to the specific drug product, it may be included on the principal display (main) panel of the inner and outer labels. Where no standard has been prescribed but a pharmacopoeial standard exists (see Section 3.4.3.2, "Pharmacopoeial Standard") and it applies to the standard proposed by the manufacturer for the specific drug product, the principal display (main) panel of the inner and outer labels may include the publication containing the standard used.

3.4.3.1 Prescribed Standard

The *Act* states:

Where a standard has been prescribed for a drug, no person shall label, package, sell or advertise any substance in such a manner that is likely to be mistaken for that drug, unless the substance complies with the prescribed standard. (Subsection 10(1))

A prescribed standard is a standard prescribed by the *Regulations*. A list of Canadian Standard Drugs (CSD) can be found in Division 6 of the *Regulations.*

Drug products containing these drug substances as single ingredients may be sold only if they conform in all aspects to that standard. A pharmacopoeial or manufacturer's standard cannot be used for these drug products.

3.4.3.2 Pharmacopoeial Standard

The *Act* states:

Where a standard has not been prescribed for a drug, but a standard for the drug is contained in any publication referred to in Schedule B, no person shall package, label, sell or advertise any substance in such a manner that is likely to be mistaken for that drug, unless the substance complies with the standard. (Subsection 10(2))

Pharmacopoeial standards are for those drug products contained in the publications listed in Schedule B to the *Act* and for which no standard has been prescribed in the *Regulations*.

When a pharmacopoeial standard is declared on the drug product label, the labelling provisions that are included in the section of the official monograph and those that are required by the general notices of the pharmacopoeial standard should be met.

When a pharmacopoeial standard is declared, the drug product must meet the current version of the pharmacopoeia. A manufacturer/sponsor cannot claim to meet a previous version of the pharmacopoeial standard.

3.4.3.3 Manufacturer's Standard

A manufacturer/sponsor may choose to manufacture a drug product to the pharmacopoeial standard (e.g., USP) or to the manufacturer's own standard and label the product as a house standard (e.g., manufacturer's name standard).

A manufacturer's/sponsor's use of a house standard on a label indicates that the drug product may differ in some respect from the pharmacopoeial standard. Sponsors can refer to their own standards as house, firm, or manufacturer's standard.

The following expressions are considered acceptable to describe a manufacturer's standard:

- House Standard, or House Std.
- Manufacturer's Standard or Mfr. Std.
- Firm X Standard or Firm X Std.

3.4.3.4 Professed Standard

The *Act* states:

Where a standard for a drug has not been prescribed and no standard for the drug is contained in any publication referred to in Schedule B, no person shall sell the drug, unless:

a. it is in accordance with the professed standard under which it is sold; and
b. it does not resemble, in any manner likely to deceive, any drug for which a standard has been prescribed or is contained in any publication referred to in Schedule B. (subsection 10(3)).

This section refers to non-official drug products for which no standard prescribed in the *Act* or *Regulations* or pharmacopoeial standard exists. The "professed standard" refers only to the label claims for quality and potency, and manufacturers/sponsors are required to set their own standards within certain limits outlined in the *Regulations*.

The label of such drug products should not carry any standard (e.g., "house standard" or "name of company standard)" as this may give the misleading impression that the product meets a prescribed or pharmacopoeial standard. The words "professed standard" should not be displayed on the labels.

It is not mandatory to declare a standard for the drug product's ingredients. However, if a manufacturer/sponsor chooses to do so, the manufacturer/sponsor must ensure that the ingredient is contained in the current edition of the pharmacopoeoia that is referred to and should not be shown on the main panel of the label, as it might be mistaken for a pharmacopoeial standard for the drug product.

3.4.3.5 Placement of Standard on Labelling

Where a standard of manufacture is shown on a label, it should be declared near the prescribed or proper name of the drug product. The quantitative amounts may be indicated before or after the prescribed or proper name (e.g., Conjugated Estrogen Tablets CSD 1.25 mg, Acetaminophen Tablets USP, 325 mg).

3.4.3.6 Updating Standards

Where a pharmacopoeial standard has been updated and the manufacturer/sponsor has been declaring that standard for that drug product or ingredient, it is the manufacturer's/sponsor's responsibility to update the processes and specifications of that product or ingredient, and to submit the appropriate submission where required.

3.4.3.7 New Pharmacopoeial Standards

Where no standard existed previously and a new pharmacopoeial standard has been created for an ingredient or drug product and where the standard applies to the manufacturer's/sponsor's product, it is the manufacturer's/sponsor's responsibility to adjust the drug product or specifications to meet or exceed the standard and to revise the labelling if required.

3.4.3.8 Pharmacopoeial Standards for Modified-Release Dosage Forms

If an immediate-release drug product is listed in a Schedule B publication and there is not a Schedule B monograph for the modified-release form of the product (e.g. delayed-release or extended-release), the modified-release product should be considered a Professed Standard (i.e. cannot declare a pharmacopoeial standard).

3.4.4 Sterility

Where a drug product is required to be sterile by the *Regulations* (section C.01.065), then the notation "sterile" "(stérile)" must normally[6] be shown on the principal display panel of the inner and outer label in accordance with section C.01.004 (1) (*a*) (v).

3.4.5 Scheduling Symbols or Pr for drugs containing an ingredient listed in the Prescription Drug List

Pursuant to section C.01.004 (1) (*b*) of the *Regulations*, the appropriate symbol for drug products listed in the Schedule to Part G to the *Regulations*, the schedules to the *Narcotic Control Regulations* and the *Benzodiazepines and Other Targeted Substances Regulations* or containing an ingredient listed in the Prescription Drug List must appear in the upper left quarter of the principal display (main) panel of the label. Refer to the appropriate regulation for specific requirements concerning size, colour, and shape of the symbols.

When a drug product contains a combination of ingredients from two or more of the schedules or ingredients listed in the Prescription Drug List, only the scheduling symbol corresponding to the more stringent control is required on the label. In these instances, the *Narcotic Control Regulations* are the most stringent, followed by the *Controlled Drug and Substances Regulations*, the *Benzodiazepines and Targeted Substances Regulations,* and the Prescription Drug List.

The one exception to the above interpretation is when the narcotic present in the combination is codeine in an amount that does not require a prescription (e.g., 8 mg). In this instance, the symbol "N" is required and, depending on the other ingredients, possibly a "C" symbol or the "Pr" symbol. If the drug product bears a "C" or "Pr" symbol, then a prescription is still required.

3.4.6 Drug Identification Number

The principal display panel of the inner and outer label of a drug product sold in dosage form (a form in which it is ready for consumer use without requiring further manufacturing) must normally[7] show the DIN assigned and preceded by the words "Drug Identification Number" or "Drogue identification numérique," or both, or the letters "DIN" (*Regulations*, section C.01.005(1)).

3.5 Any Panel

This subsection provides further detailed information to be included on any other panel of an inner and outer label.

3.5.1 Name and Address of Manufacturer/Sponsor

Pursuant to Section A.01.10 of the *Regulations*, the manufacturer/sponsor or distributor is the "person," including an association or partnership (which can also mean business or corporation under that name), that sells a drug product (i.e. owns the DIN). The manufacturer/sponsor or distributor can own the DIN. The manufacturer is not necessarily the fabricator. Where more than one name appears on the label, each person mentioned may be held responsible for compliance with the requirements of the *Act* and *Regulations*.

The *Regulations* require that the label display the name and address of the manufacturer/sponsor or manufacturers/sponsors (Section C.01.004). If the address shown is not Canadian, then the name of the Canadian importer and the name and address of the distributor must be added (Section C.01.004.1*)*. The importer and distributor may be two (2) separate entities or they could be the same, in which case only a single name and address showing the responsible Canadian agent needs to be shown on the label.

The address should be sufficiently complete so that Canada Post could deliver a letter mailed to that address. For Canadian manufacturers/sponsors, it may suffice to have the name of the city and province. For distinct cities, the province may be omitted and "Canada" used instead. The postal code should be included in all

cases. Any non-Canadian addresses that appear on the label should include the name of the country. Refer to the Canada Post Addressing Guide for more information (www.canadapost.ca).

The address must be sufficient to ensure delivery of a letter through the various postal systems involved in the delivery.

For prescription products and those obtained or administered through a health professional, as of June 13, 2015, C.01.004.01(1) requires contact information in Canada to report 'harms' that may be associated with the product. For further information on the type of contact information and language to be included, see section 2.1.2 of this *Guidance*.

3.5.2 Lot Number

The lot number may be any combination of letters, figures, or both (section A.01.010 of the *Regulations*) by which a drug product can be traced to the manufacturer/sponsor and, if applicable, to the distributor or importer. This number should be preceded by the words "Lot Number" or a suitable abbreviation (i.e. Lot No., Lot, L.), and must appear on any panel of the inner and outer labels (section C.01.004 (1) (*c*) (ii)).

An appropriate designation for a lot number should be shown on all submitted draft labels to clearly indicate the manufacturer's/sponsor's intent to add the lot number to the label at the time of packaging (e.g., filling).

3.5.3 Expiration Date

The expiration date must be on the inner and outer labels of all drug products (section C.01.004. (1)(*c*)(v)). The *Regulations* currently do not specify a particular wording or expression for expiry date. However, some acceptable terms include "Expiration" or "Expiration date" in English, and "Expiration" or "Date d'expiration" in French. The term "Expiration" or its abbreviation "EXP." is acceptable as a bilingual expression.

The expiration date should be expressed in full or in any manner that the general public or end user will clearly understand. To provide consistency, the use of the pattern: year, month and day established in the foods section of the *Food and Drug Regulations* is suggested. Acceptable abbreviations are the last two digits of the year (under the circumstances identified below), two letters for the month, and two digits for the actual day of the month, if required.

The following patterns to express the expiry date are optional; however, Health Canada recommends this format in drug product labelling:

1. If the expiry date includes the year and month, the four digits of the year and two letters of the month (e.g., 2009 AL) **or** the two digit year and two letters of the month (e.g.,09AL) should appear on the label, with the last day of the month assumed.
2. If the expiry date includes the year, month and day, the four digits of the year, the two letters of the month and the two digits of the actual day of the month (e.g., 2009AL30) **or** the four digits of the year, the full month written out, and the two digits of the actual day (e.g., 2009 April 30) should appear on the label.

As provided in section B.01.007of the *Regulations*, the following two-letter abbreviations for the months are acceptable in both official languages: JA, FE, MR, AL, MA, JN, JL, AU, SE, OC, NO, DE.

An appropriate designation for an expiration date should be shown on all submitted draft labels to clearly indicate the sponsor's intent to add the expiration date to the label at the time of packaging (e.g., filling).

3.5.4 Adequate Directions for Use

Section C.01.004. (1) (*c*) (iii) of the *Regulations* requires that that the inner and outer labels show "adequate directions for use of the drug product." This is interpreted to include:

1. indications for use or pharmacological classification;
2. recommended single and daily dose;
3. route of administration, when the route is not obvious;
4. any warning or cautions specifically required by the Regulation; and
5. storage conditions.

More detailed information that may be necessary for the proper use of the drug product by the consumer, but for which there is no room on the label, must be provided in some additional labelling such as a consumer information document.

For a prescription drug product, this consumer information may be a package insert or a document provided to the patient at the point of dispensing. The manufacturer/sponsor generated label should include a statement regarding the availability of this document, such as, "See consumer information [leaflet]" or "Pharmacist (or Doctor[8]): Dispense with consumer information [leaflet]."

For a non-prescription drug product, the consumer information should be provided as a package insert. The inner and outer labels should include an instruction to consult the package insert for further directions, such as, "See consumer information [leaflet]."

For a new drug, subject to the requirements of Part C, Division 8, of the *Regulations*, the inner and outer labels should include a statement regarding the availability of the Product Monograph, such as, "Product Monograph available on request."

For prescription drug products that are not considered new drugs subject to Part C, Division 8 of the *Regulations*, the label should include a statement regarding the availability of the prescribing information, such as "Prescribing Information available on request" (see section 5.4.5) or "See package insert" where such a document exists. This is especially important when there is not enough space on the label for more detailed drug information that may be required by the healthcare professional for the safe and effective use of the drug product.

For any prescription drug product where substantial product preparation may be required by the healthcare professional before dispensing (e.g., reconstituting parenterals), sponsors/manufacturers should consider including the prescribing information as a package insert. In this case the label should include a statement such as, "See package insert" (refer to section 5.4.2 of this guidance).

For labels showing a claim, indication or reference for a Schedule A disease, see section 2.7 of this guidance.

Health Canada recommends that positive statements should be used on labels to avoid ambiguity, wherever possible. For example, "For subcutaneous use only" is preferred over a negative statement such as "Not for intravenous use." However, it is recognized that some negative statements in warnings are very effective and will continue to be used (e.g., "Do not take Drug Product B while taking Drug Product A").

3.5.4.1 Storage Conditions

Storage conditions are considered to be part of adequate directions for use, where applicable, and must be shown on the inner and outer labels (section C.01.004. (1) (*c*) (iii)). Guidance on appropriate storage conditions assists patients, consumers and healthcare professionals in maintaining product quality and safety.

3.5.4.2 Limit Dose Drug Products

For drug products that carry a recommended single or daily dose or statement of concentration above the limits provided by section C.01.021 of the *Regulations*, the inner and outer labels must state that the product is to be used only on the advice of a physician (section C.01.025).

3.5.4.3 Warnings and Precautions

The *Regulations* require several cautionary statements, such as those for acetylsalicylic acid and salicylic acid. Cautions shown within quotation marks in the *Regulations* must be printed verbatim. If the caution or warning does not appear within quotation marks, the wording may be altered but the meaning must be retained. Additional warnings and cautions outside the *Regulations* and specific to the drug product or drug product class may also be required on labels to help ensure safe use of the drug product.

3.5.5 Declaration of Medicinal Ingredients

Except as otherwise provided in the *Regulations*, pursuant to section C.01.004(1)(*c*)(iv), the quantities of all medicinal ingredients must normally be declared[9] on the inner and outer labels with the ingredients listed by their proper names or, if there are no proper names, by their common names. The standards of each individual ingredient should not be declared on the main panel of the label of a multi-ingredient drug product as it misleadingly implies a pharmaceutical standard for the combination. However, when a standard exists for the entire combination, then this standard may be declared on the main panel of the label.

Except as otherwise provided in the *Regulations*, the method of declaring the quantities of active ingredients should be as described in the following table.

Table 3.1: Method of Declaring Quantities of Active Ingredients

Pharmaceutical Form	Appropriate Declaration
Tablets, capsules, suppositories and other discrete dosage forms	gram (g) or milligram (mg) per dosage form
Powders for oral use	gram (g) or milligram (mg) per gram, **and** per specific dosage unit (for example, level teaspoonful)
Liquids for parenteral use[10]	milligram (mg) per millilitre (ml), or % weight per volume (w/v)
Liquids for oral use	gram (g) or milligram (mg) per dosage unit, or per millilitre (ml)
Creams, lotions, ointments	milligram (mg) per gram (g)(= mg/g or % w/w), or milligram per millilitre (= mg/ml or %w/v)

Leading and Terminal zeroes

The use of terminal (trailing) zeroes following a quantitative declaration of the medicinal ingredient should be avoided. Use 2 g rather than 2.0 g and 2.5 g instead of 2.50 g to avoid confusion.

When a quantitative amount is expressed as a decimal number less than 1, then the declaration should be preceded by a leading zero, such as 0.5 mg.

3.5.5.1 Non-parenteral Products Requiring Dilution

For non-parenteral drug products that must be diluted prior to use (e.g., powders for reconstitution), the inner and outer label should indicate the:

1. quantity of medicinal ingredients per container;
2. final concentration after reconstitution (e.g., mg per millilitre [mL]); and
3. identity of the diluent and the quantity to be added for reconstitution.

Where percentages are used, they should be specified as % w/w, w/v, or v/v, as applicable.

3.5.5.2 Single Ingredient Preparations

When a drug product contains a single medicinal ingredient, a declaration of the quantity of medicinal ingredient immediately following or preceding the proper or common name of the drug product is acceptable, provided that the amount refers to the medicinal ingredient in the form mentioned in the name. Examples: Acetylsalicylic Acid Tablets 300 mg or Hydrocortisone Acetate Ointment 1% w/w. In the second example, the product is understood to contain 1% w/w Hydrocortisone Acetate and not 1% w/w Hydrocortisone.

The declaration of the medicinal ingredient should reflect how the strength of the drug product is expressed. For example, if the proper name of the drug product is Chloramphenicol Palmitate Oral Suspension and the strength is expressed in terms of milligrams per millilitre of the chloramphenicol, then an acceptable quantitative declaration of the medicinal ingredient would be "Chloramphenicol 30 mg/mL as Chloramphenicol palmitate".

3.5.5.3 Combination Immediate Release/ Modified Release Ingredients

A combination drug product may contain an immediate release medicinal ingredient along with modified-release medicinal ingredient in the same pharmaceutical form (e.g., tablet). In these instances, the dosage form should be clearly labelled to reflect the combination.

3.5.5.4 Transdermal Patches

The inner and outer labels (e.g., pouch and carton) of transdermal patches should include a declaration of the total quantity of the medicinal ingredients per patch, the mean dose delivered per unit of time (e.g., X mg/day, X mg/hour), and the duration of patch use (e.g., Y hours, Y days).

To ensure the proper identification of these drug patches, especially to inform healthcare personnel in cases of inadvertent contact with these discarded patches by children and pets, the patch itself should be labelled with the following minimum information:

1. Brand name;
2. Common or proper name;
3. Quantitative declaration of the medicinal ingredients;
4. DIN; and,
5. Delivery rate of the drug (e.g., X mg/hour).

3.5.5.5 Implants

Labelling for implants (e.g., wafers, capsules, and pellets), should include the total quantitative declaration of the medicinal ingredients per implant, the mean dose delivered per unit of time (e.g., X mg/day), and the duration of use (e.g., Y days).

3.5.6 Declaration of Non-medicinal Ingredients

Amendments to the *Food and Drug Regulations*, effective May 13, 2012, modify section C.01.004 of the *Regulations*, to state:

(1.1) "...when a drug is intended for human use, its outer label must contain a list of all nonmedicinal ingredients, or, if the outer label is too small, the list must appear on a tag, tape or card that is attached to the package."

(1.2) "The nonmedicinal ingredients must be listed in alphabetical order or in descending order of predominance by their proportion in the drug, preceded by words that clearly distinguish them from the medicinal ingredients."

(1.4) When the composition of the drug varies from one lot to another, the outer label must include a reference to all non-medicinal ingredient alternatives that may be present in the drug, preceded by the symbol "+/-" or "±" or the expression "or/*ou*" or "may contain/*peut contenir.*"

The above is intended to apply to non-prescription drug products and does not apply to:

a. prescription drug products;
b. drug products not required to be sold pursuant to a prescription but are administered under the supervision of a healthcare professional; or
c. veterinary drug products and hard-surface disinfectants, both of which are outside the scope of this label guidance.

A complete listing of all nonmedicinal ingredients on the label of a non-prescription drug product increases patient safety and better informs the consumer and healthcare professional in deciding the most appropriate drug product for each patient.

The non-medicinal or inactive ingredients should be clearly separated from the medicinal ingredients with a heading such as "nonmedicinal (inactive) ingredients". These nonmedicinal ingredients should be identified by the common or proper name.

Nonmedicinal ingredients should be generally excluded from the drug product name. Exceptions can be made with respect to flavour, colour, fragrance or non-therapeutic purposes provided this purpose is specified in the brand, or product name. A nonmedicinal ingredient which forms part of the brand name should be clearly identified with the cosmetic, non-therapeutic purpose within the brand name (e.g., Sunscreen X with moisturizing aloe) unless the non-therapeutic benefit is obvious (e.g., Antiseptic Raspberry Mouthwash [raspberry flavour]).

Where a manufacturer/sponsor of a prescription drug product chooses to list nonmedicinal ingredients on the label (optional), then the non-medicinal ingredients should be similarly and clearly identified by the common or proper name and identified as nonmedicinal or inactive ingredients.

3.5.6.1 Different Flavours, Colours, or Fragrances

A single DIN is assigned for drug products varying in flavour, colour, or fragrance, provided that all other product characteristics including: formulation, route, dosage form, product name, manufacturer's/sponsor's name, and labelling are identical. Refer to the Health Canada policy document, *Drug Identification Number: A Brand Name Product with Different Fragrances, Flavours or Colours*, for more information. For details concerning flavours, fragrances, and variable formulations, refer to the new regulations regarding nonmedicinal ingredients (see Appendix B).

3.5.6.2 Colouring Agents

The use of colouring agents in drugs is restricted to those listed in section C.01.040 of the *Regulations*. If a manufacturer/sponsor wishes to use a new colouring agent not listed in section C.01.040, safety data for the

new colouring agent must be submitted to Health Canada for review and approval before use. Only the names listed in the *Regulations* may be used (section C.01.040) in drug product labelling.

Note that with regulatory changes discussed in section 3.5.6, manufacturers/sponsors must declare all colouring agents on the labels of non-prescription drug products effective May 13, 2012. (See Appendix B).

3.5.6.3 Nomenclature for Non-medicinal Ingredients

Health Canada's policy *Non-medicinal Ingredients Nomenclature* outlines the accepted nomenclature used in naming the non-medicinal ingredients in drug product formulations. The list is not all-inclusive and does not imply acceptability for use in the labelling of all drug products; therefore, it should be used as a guide only.

3.5.7 Net Amount (Net Contents)

Net contents must be declared on the outer label as outlined in section C.01.004 (2) (*a*) of the *Regulations*. In some cases, however, it may be desirable to have this information on the inner label also. Manufacturers/sponsors should consider whether repeating the information would be useful in administration of the drug product. Standard units of measure and abbreviations (e.g., ounces, oz.), may also be included on the label in addition to the required metric units.

3.5.8 Preservatives

For drug product lines containing ophthalmic or parenteral drug product formulations, and where two products differ only in the presence or absence of a preservative, the label should clearly identify the presence or absence of a preservative, either by reference in the brand name or directly and prominently on the label. Health Canada will issue two separate DINs to emphasize the difference in drug product identity.

3.6 Special Packaging

The following subsections provide labelling requirements for special types of packaging.

3.6.1 Co-packaged Products

Co-packaged products containing two different drug products, or a drug and a non-drug item (e.g., cosmetic and device) must comply with the regulatory requirements for each product. As the co-packaging of certain drugs products may imply certain unapproved claims, pose a safety concern, or require the filing of a New Drug Submission (NDS), manufacturers/sponsors should consult with Health Canada prior to marketing co-packaged products.

The labelling of co-packaged drug products must include only those claims and indications that have been authorized for the individual drugs. If claims for the drug product exceed the authorized claims for the components, or new claims are made on the concomitant administration of the drug and non-drug product, then the manufacturer/sponsor must file a drug submission for the new combined use.

With respect to filing these drug submissions, manufacturers/sponsors may wish to consult the various Health Canada documents mentioned in Appendix B, such as:

(a) For Division 8 drugs (i.e. New Drugs): Guidance for Industry: Post Notice of Compliance (NOC) Changes; or
(b) For Division 1 drug[11]: Guidance for Industry: Post Drug Identification Number (DIN) Changes.

3.6.2 Labelling of Drug Products in Small Containers

The labelling requirements for drug products generally apply to all container sizes. However, some containers are too small to show all the information required by the *Act* and *Regulations*. Section C.01.004 (3) of the *Regulations* addresses this issue as follows:

Where the container of a drug is too small to accommodate an inner label that conforms to the requirements of these *Regulations*, the inner label requirements of these *Regulations* do not apply to the drug in that container if:

(a) there is an outer label that complies with the labelling requirements of these *Regulations*; and
(b) the inner label shows
    (i) the proper name of the drug, the common name of the drug if there is no proper name or, in the case of a drug with more than one medicinal ingredient, the brand name of the drug,
    (ii) the potency of the drug except where, in the case of a drug with more than one medicinal ingredient, the name used pursuant to section (i) for that drug is unique for a particular potency of the drug,
    (iii) the net content of the drug if it is not in a discrete dosage form,
    (iv) the route of administration of the drug if other than oral,
    (v) the lot number of the drug,
    (vi) the name of the manufacturer/sponsor of the drug,
    (vii) the expiration date of the drug, and
    (viii) the identification of special characteristics of the dosage form if they are not evident from the name of the drug under sections (i) or (ii).

3.6.3 Labelling of Special Containers

Drug products may be packaged in special containers that are too small to accommodate an inner label that conforms to the requirements of subsection C.01.004 (3) of the *Regulations*. This inner label may contain further abbreviated labelling, provided there is an outer label that meets all regulatory requirements. The two types of packages are:

- Multiple-dose packs, such as: blister packs, strips, push-through cards, ampoules, or vials attached by a plastic strip; and
- Single-dose packs, such as: sachets, pouch-type packs, individual dose vials of liquid or pre-packaged syringes.

These packages should contain the information listed in Subsections A and B below, and as outlined in the Health Canada policy document, *Labelling of Special Containers*. Consideration should be given to the colour of the text and the use of non-reflective or coloured foils that may enhance the legibility of the text for these special containers.

A. Multi-dose Containers

Labels for multiple-dose packs should include, at a minimum, the following information:

- Brand name or if no brand name, then the proper or common name plus the manufacturer's/sponsor's name;
- Potency of the drug except where, in the case of a drug with more than one medicinal ingredient, the name used is unique for a particular potency of the drug; and
- Lot number and expiry date.

The above information should be presented in a way that ensures that the package information is maintained and can be read after units have been removed. This can be achieved by printing in a repetitive manner or by embossing on the edge of each card.

B. Single Dose Containers

Labels for single-dose packs should include the same information as labels for multiple-dose packs (See A), but if there is insufficient space, the expiry date may be omitted.

For drug products containing multi-ingredients (e.g., cold product with four ingredients) where the blister package label may not accommodate the quantitative amount of each ingredient as required by the *Regulations*, the use of a brand name unique for a particular potency is acceptable. If a brand name is not unique for a particular potency, it is acceptable to have the brand name and the DIN appear on the blister package label (e.g., Cough/Cold Tablet, DIN 12345678), which clearly identifies the drug product.

Although a DIN is not required on the labels of small containers described in this section 3.6.3, it is still highly recommended as an added safety precaution if space is available.

3.6.4 Security Packaging

Pursuant to section A.01.065 of the *Regulations*, drug products intended for ingestion, inhalation, or insertion into the human body, mouthwashes, or drug products intended for ophthalmic use, must be contained in a security package if the drug product is available to the general public in an open selection area. The labels on these products must draw attention to the security feature of the package. For further information, refer to the *Regulations*, section G.02.019 (*c*) for controlled drugs and section J.01.030 for restricted drugs.

3.6.5 Drugs in Pressurized Containers and Flammability

Drug products packaged in a disposable metal container designed to release pressurized contents by the use of a manually operated valve must show the cautionary statements, hazard symbols, and signal words as outlined in sections A.01.061 to A.01.063 of the *Regulations*.

Drug products packaged in unpressurized containers operated by a manual pump spray device or any other containers that contain flammable ingredients should show a cautionary warning indicating flammable contents and appropriate directions for use (e.g., "Do not use near an open flame").

3.7 Technical Information and Language

Technical information should be presented in terminology that is easily understood by the consumer. The amount of information provided should not exceed that required to arrive at a proper conclusion. Technical information is more likely to mislead or deceive the consumer in controversial areas where scientific opinions diverge. Technical or complicated language should not be used to purposely obscure, disguise, or exaggerate drug product benefits.

With the new requirement to include a Part III, Consumer Information document for all new drugs in the new Product Monograph format (see the *Guidance for Industry: Product Monograph*), there is an increase in technical information that has to be explained to consumers. A balance is required between exposure to sufficient information for safe, effective, and informed use of a medication versus too much information, which could overwhelm the consumer. For some prescription drug products there is no accurate consumer language to describe some conditions; therefore, the original technical language must be maintained, while attempting to explain the condition in a way the consumer would understand.

Technical information, when required, should be written:

1. in language at no greater than a Grade 8 reading level;
2. in simple, clear, and easy to understand language; and
3. presented with numerous headings and bulleted points.

Manufacturers/sponsors may wish to refer to the Canadian Public Health Association's guidance, Good Medicine for Seniors: Guidelines for Plain Language and Good Design in Prescription Medication on plain language for drug labelling (see Appendix C).

3.8 Labelling of Professional Samples

Subsection 14(1) of the *Act* prohibits the distribution of any drug as a sample, which is considered to be a package of a drug provided at no cost. However, subsection 14(2) allows the "distribution, under prescribed conditions, of a sample to physicians, dentists, veterinary surgeons, or pharmacists." The conditions that must be met are provided in sections C.01.048 and C.01.049 of the *Regulations*.

A sample of a drug product given to a healthcare professional and intended for subsequent distribution to a patient, must be labelled with the same directions required for the safe and effective use as for regular package sizes of prescription and non-prescription drug products. All labelling that is normally distributed with the regular package sizes should be distributed with samples, including the consumer information document for all new drugs in the new Product Monograph format.

It is understood that the labelling detail required for a non-prescription drug product may be greater than that required for a prescription drug. Refer to the Health Canada policy document *Labelling of Professional Samples of Drugs.*

3.9 Including International Information on Drug Package Labels

Package labels (inner and outer) for drug products authorized for sale in Canada may include additional regulatory information approved by other regulatory jurisdictions (e.g., NDC number) provided that the label:

- meets Canadian regulatory requirements;
- is consistent with applicable Health Canada guidance documents and policies;
- does not cause confusion and;
- is consistent with the terms of market authorization for the drug product (e.g. a prescription symbol required in another country should not appear on the Canadian label of a product which is non-prescription in Canada).

4. Claims and Text Content

Subsection 9(1) of the *Act* prohibits the representation of a drug "in a manner that is false, misleading or deceptive or is likely to create an erroneous impression regarding its character, value, quantity, composition, merit or safety." Drug manufacturers/sponsors can ensure drug product labelling complies with the *Act* by providing accurate and concise information to assist healthcare professionals in choosing the correct medication for patients, and consumers in identifying the availability and effects of therapeutic agents for self-medication.

Drug products, due to their potential risk, should be labelled in an informative manner. It is the manufacturer's/sponsor's responsibility to periodically update product labels to be consistent with current scientific information and medical treatment.

4.1 Misrepresentation of Classification

Labelling should clearly indicate that the product is a drug. Sponsors should avoid describing the drug product, its purpose, or method of use in a way that implies it is another product type, such as a food or cosmetic. Misrepresentation of classification can create an erroneous impression regarding the character, merit, and safety of a preparation (e.g., medicated versus cosmetic shampoo).

4.2 Absence of Ingredients

Consumers and patients may be concerned about the health implications of certain medicinal and non-medicinal ingredients in drug product formulations (e.g., sugars, salts, sulfites). Manufacturers/sponsors may selectively refer to the absence of certain ingredients under particular conditions (e.g., no ingredient X, no X, non-X, X-free).

When an ingredient has been removed from drug products in Canada because of safety concerns, it is acceptable to include a statement to the effect that a drug has been reformulated to omit that ingredient or that the drug product does not contain that ingredient. Such statements are considered acceptable for a limited time (e.g., one year), but after a certain period they lose meaning as the unacceptable ingredient is no longer found in other products.

For example, phenylpropanolamine as a non-prescription oral decongestant has been removed from drug products in Canada because of safety concerns. As phenylpropanolamine is no longer found in any over-the-counter oral decongestant, a "PPA-free" claim is no longer relevant or acceptable as a claim for this drug product class.

Because such statements are intended to reinforce consumer acceptance of drug products, such statements would be acceptable for preparations that previously contained the subject ingredient and that belong to that class of products in which the subject ingredient could be expected. For further guidance, refer to the Health Canada policy document, *Absence of Ingredient Statements for Non-prescription Drugs*.

4.2.1 Sugar-free, Sucrose-free, Sweetener-free

Label statements such as "sugar-free" are acceptable only for those drug products that do not contain any of the chemical classes of sugar, including sugar alcohols. If the label bears a "sugar free" claim or equivalent, and if a sweetening agent or agents are present, then the drug product label should include a phrase such as "sugar-free- sweetened with agent X (or Agents X, Y, Z..... including sugar alcohols)." This accompanying statement will reduce the risk of misleading consumers.

Health Canada suggests that drug product labels claiming one of the sugar alcohols specify the number of energy calories provided per dose.

Claims such as sweetener-free, artificial sweetener-free, and artificial sweetener X-free may be acceptable if true. However, claims for the absence of a particular artificial sweetener (e.g., "aspartame-free") may be misleading if it is not revealed to the consumer that the drug product may contain another artificial sweetener (e.g., acesulfame potassium). In these situations, the declared absence of one sweetener should be accompanied by the equally prominent declaration of the actual sweetener used.

4.2.2 Salt and Sodium-free

Drug products without sodium chloride may be labelled as "salt-free," while those without sodium may be labelled as "no sodium." The expressions "low salt," "low sodium," "suitable for low sodium diets," or "suitable for restricted sodium diets" are acceptable if the daily amount of sodium provided by the drug product is 25 mg or less.

4.3 Absence of Side Effects

Some consumers wish to avoid some specific side effects that can occur with some non-prescription drug products, but not others within the same product class (e.g., some antihistamines have a likely somnolent side effect while others are non-drowsy). Statements regarding the absence of a side effect are permitted provided the following conditions are met:

Scientific evidence exists to support the statement, such that the incidence of a side effect is comparable to when a placebo is taken. Scientific evidence to support the statement should be available to the manufacturer/sponsor and submitted to the Health Canada upon request. The evidence would consist of data from well-designed clinical trials, including sufficient sample sizes and adequate control groups, such that a significance level of 0.05 is attained and the study meets the 80 to 90% power test for excluding Type I and Type II errors. The substantiating data should include results derived from measurable, objective parameters, where feasible. If the incidence of a particular side effect exceeds that for the placebo, the statement regarding the absence of side effects should not be used.

There is a widely held consumer perception that the significant side effect is associated with comparable drug products of that class. For example, drowsiness is a side effect perceived to be frequently associated with the use of non-prescription cough and cold products. A claim indicating the absence of this side effect for a drug product within this product class, would be acceptable provided all other conditions are met.

The claim regarding the absence of a side effect provides practical consumer information so that consumers can readily identify the side effect or benefit.

Statements about the presence of significant adverse effects are accorded equal prominence in the labelling material to statements about the absence of side effect. The colour, contrast, position, and spacing of the information should be considered when assessing the requirement for equal prominence.

No undue emphasis on the statement about the absence of side effects is presented in labels or advertising. Statements regarding the absence of side effects should be submitted via the Post-NOC Changes process for new drugs and via the Post Drug Identification Number (DIN) Changes process for drugs that are Division 1 drugs[12]. Health Canada recommends that prior approval be obtained concerning the use of these statements for all drug products.

It is the manufacturer's/sponsor's responsibility to ensure that all such claims remains valid. If any of the scientific information changes then these claims should be removed.

4.4 Side Effects and Placebo Comparisons

Comparisons of the incidence of side effects on labels between the drug product and placebo are often misleading and should be avoided. For example:

In clinical studies, frequent side effects observed more often with Ingredient X than the placebo (sugar pill), were headache and diarrhea. Other side effects observed about as often on Ingredient X as on the sugar pill, included abdominal pain, nausea, flatulence, dizziness, back pain, and influenza-like symptoms.

This text requires an ability to evaluate two different comparisons and assess their significance, which may be difficult for some consumers. The message should be as simple and straightforward as possible, limited to the side effects that are reasonable to expect. More appropriate wording would be, "Frequent side effects were headache and diarrhea." Manufacturers/sponsors may also choose to include the other side effects, without citing the comparison with the placebo.

4.5 Look-alike, Sound-alike Drug Product Names

For prescription products and those administered or obtained through a health professional, as of June 13, 2015 there are new regulatory requirements under C.01.014.1(2)(*o)* and C.08.002(2)(*o)* for submissions regarding product names. These requirements specify the need for an assessment as to whether there is a likelihood that the drug will be mistaken for any of the following products due to a resemblance between the brand name that is proposed to be used in respect of the drug and the brand name, common name or proper name of any of those products:

i. a drug in respect of which a drug identification number has been assigned,
ii. a radiopharmaceutical, as defined in section C.03.201, in respect of which a notice of compliance has been issued under section C.08.004 or C.08.004.01, and
iii. a kit, as defined in section C.03.205, in respect of which a notice of compliance has been issued under section C.08.004 or C.08.004.01.

Look-alike, sound-alike (LA/SA) refers to names of different health products that have orthographic similarities when written or similar phonetics when spoken. These similarities may pose a health risk by causing confusion in the prescribing, dispensing, administration of a drug product, or in the selection of a non-prescription drug product by the consumer. It is the manufacturer's/sponsor's responsibility to ensure that any proposed brand name will not cause potential confusion with another brand name, common or proper name. The manufacturer/sponsor should perform an analysis and risk assessment for any proposed product name to support its use.

For prescription products and those administered or obtained through a health professional, please refer to: *Guidance for Industry: Review of Drug Brand Names* and the *Frequently Asked Questions - Guidance Document for Industry - Review of Drug Brand Names*.

4.6 Comparisons

Manufacturers/sponsors are encouraged to promote drug products on their own merits in a positive manner instead of by comparison with other products. Comparisons with other drug products or with the selected properties of other drugs are potentially misleading. The consumer, while competent to evaluate comparisons of taste, flavour, colour, and appearance, generally lacks the expertise and access to the supporting data required to evaluate the implications of comparisons about the therapeutic properties of drug products. Manufacturers/sponsors should exercise caution when presenting comparative statements to the public to avoid being in contravention of subsection 9(1) of the *Act.*

Comparisons may be misleading for several reasons:

- Comparisons are generally incomplete. Usually, only the advantages of the advertised drug product and the disadvantages of the competitive product are mentioned. Special benefits or advantages of the competitive product are generally omitted.
- Comparisons exaggerate the importance of the alleged advantages of the drug product (e.g., speed of action, quantity of medicinal ingredient, or extent or duration of action). Failure to disclose the lack of real therapeutic advantage is often deceptive.
- Differences of opinion between experts regarding the truth and impact of the compared qualities are often undisclosed.

4.6.1 Implied Comparisons

Some terms and phrases used to describe the composition of drug products imply comparisons that convey an erroneous impression regarding a product's value and merit. The terms "better," "richer," and "stronger" indicates an unidentified comparison which may be misleading and implies product superiority when this may not be the case. Where a drug product has been reformulated to be significantly more effective or to provide an additional therapeutic advantage over a previous formulation, the use of "better" may be acceptable, if carefully explained. However, it should be clearly indicated that the drug products being compared are the old and new formulations. To avoid violating subsection 9(1) of the *Act*, sponsors should describe such a product as a "new" or "improved" formulation. The use of such terms to describe novel or modified products is acceptable for one year.

4.6.2 Therapeutic Comparative Claims

Therapeutic claims are those related only to the therapeutic aspects of the drug product (e.g., therapeutic actions, efficacy, speed of action, symptom relief). For manufacturers/sponsors wishing to consider labelling or advertising that includes therapeutic comparisons to other drug products for human use, Health Canada's *Therapeutic Comparative Advertising: Directive and Guidance Document* provides:

1. broad principles applicable to all drug products for human use regardless of the intended audience (healthcare professionals or consumers);
2. detailed data requirements necessary to support consumer-directed non-prescription drug product advertising and labelling;
3. roles and responsibilities of Health Canada and the sponsor concerning labelling; and
4. roles and responsibilities of Health Canada, the sponsor, and the independent advertising preclearance agency concerning advertising.

The purpose of *Therapeutic Comparative Advertising: Directive and Guidance Document* is to provide a framework for supporting evidence and presentation of comparative therapeutic claims in labelling and advertising, to ensure these claims are not false, misleading, or deceptive to the intended user.

Manufacturers/sponsors wishing to add therapeutic comparisons to labelling, which is generally discouraged if the overall effect is considered promotional, should seek pre-approval of the label claims through the submission and approval of an appropriate change to labelling. Refer to the Health Canada's *Guidance for Industry: Post-Notice of Compliance (NOC) Changes* or *Post Drug Identification Number (DIN) Changes* documents in Appendix B.

4.6.3 Non-therapeutic Comparisons

The Therapeutic Products Directorate (TPD) is not responsible for the review of the comparative, non-therapeutic qualities claimed for drug products in labelling (e.g., taste, fragrance, colour, physical, sensory, cosmetic benefit, market share, cost effectiveness etc.) provided these claims do not conflict with the therapeutic understanding of the product.

The purpose of the existing Health Canada policy, *Principles for Claims Relating to Comparison of Non-therapeutic Aspects of Non-prescription Drug Products*, is to define the conditions under which such comparisons will not be considered false, misleading, or deceptive as to the therapeutic character, value, quantity, composition, merit, or safety of the drug product to the intended audience. This measure is to aid sponsors and the industry to create labelling and advertising in compliance with the *Act* and *Regulations*, particularly subsection 9(1) of the *Act*.

The sponsor is responsible for ensuring that the applicable non-therapeutic, comparative claims meet the requirements of Health Canada's policy. Health Canada does not accept complaints concerning overall impression of comparative, non-therapeutic claims unless these claims interfere with the therapeutic aspects of the drug product. Advertising complaints concerning these non-therapeutic comparative claims can be forwarded to the sponsor, the courts (for complaints brought under the *Competition Act*) or may be considered by industry or voluntary pre-clearance agencies.

4.6.4 High, Low

The terms "high" and "low" generally imply unidentified comparisons and standards against which a drug product must be measured. For most product classes, these standards do not exist; therefore, these terms are unacceptable. To avoid misleading the consumer regarding the benefits of a product, more specific terminology should be used.

In some specific drug product areas, such as sunscreens, where a measurable standard of comparative performance is available (e.g., SPF, sun protection factor), these terms may be accepted in a product line to assist the consumer in product choice, in addition to the principle measure of effectiveness, the SPF, which is outlined in the appropriate Health Canada labelling standards and monographs (see Section 5.2.1).

4.7 Endorsements, Testimonials, and Quotations

The following subsections provide guidance for the use of endorsements, testimonials, and quotations from the media or medical literature.

4.7.1 Endorsements, Seals of Approval

Endorsements of drug products (e.g., "doctor recommended") by healthcare professionals, celebrities, and others are acceptable in labelling provided the endorsements are consistent with the expected actions and terms of market authorization and supporting data is available (where necessary), and there is no violation of the *Act* and *Regulations*. The endorsements should also be consistent with related Health Canada guidance documents and policies.

Seals of approval on the labelling of certain drug products issued by independent professional bodies (e.g., Canadian Dental Association) may be acceptable if the written material explaining the exact nature of the endorsement has been provided to TPD for review and the products in the product class meets the independent product recognition based on certain criteria. This recognition must be consistent with the terms of market authorization of the product. TPD will conduct only one evaluation to validate the criteria used by the attesting organization. It is the manufacturer's/sponsor's responsibility to ensure that they have documentation on file that shows the drug product has obtained the endorsement from this third party organization and that the drug product continues to meet the attesting organization's criteria. Product-specific data showing that a product meets this seal of approval is not expected with a drug product submission submitted for review but must be available on request.

4.7.2 Testimonials

Testimonials or quotations from individuals on drug product labels frequently constitute an unfair and biased advantage. There may be no acceptable way of indicating on the labelling how such cases compare with the frequency of failure or success of that treatment. It may be misleading to build unwarranted expectations in

the consumer's mind by the use of success stories. However, if such testimonials are consistent with the expected benefits of the product and the terms of market authorization, they can be accepted following critical review, provided the testimonial does not otherwise violate the *Act* and *Regulations*.

4.7.3 Quotations from Media, Journals, or Texts

Quotations from scientific journals, papers, authoritative texts, magazines, newspapers, or any other media source may create an erroneous impression regarding the character, value, merit, or safety of a drug product. This material may not reflect the entire data package supporting the drug product and may represent the isolated opinion of the author or a biased selection of data; therefore, sponsors should avoid using quotations on drug labels.

4.8 Cosmetic Claims

Cosmetic claims and any description of the cosmetic or non-therapeutic attributes of the drug product (fragrance, texture, colour) are acceptable for therapeutic products provided they:

- do not directly or indirectly imply therapeutic activity;
- are not misleading as to therapeutic merit, identity, composition, and character of the drug product, or in violation of the *Act* and *Regulations* (e.g., prohibited substance); and
- have evidence available to support the cosmetic claim.

TPD will comment on any claim that the manufacturer/sponsor believes to be a "cosmetic" claim but is actually considered to be a direct or indirect therapeutic claim that may be misleading as to the merit of the drug product. TPD may consult Health Canada's National Capital Region Consumer Product Safety Bureau, Cosmetics Program concerning claims that may be difficult to classify as cosmetic versus therapeutic.

Manufacturers/sponsors are encouraged to consult the *Guidelines for Cosmetic Advertising and Labelling Claims*, available through Advertising Standards Canada (ASC), for guidance concerning acceptable cosmetic claims. Any cosmetic claim attributed to a specific ingredient (e.g., "with moisturizing aloe vera") must be supported by data on file and available to Health Canada upon request.

4.8.1 Cooling

The term "cooling" may be used in a therapeutic sense, if the drug product contains a medicinal ingredient for a therapeutic purpose such as "for cooling relief of sunburn" (e.g., topical anaesthetic with menthol or camphor). The term may also be used in a non-therapeutic sense if adequately explained (e.g., antiseptic mouthwash with a cooling sensation flavour such as menthol).

4.9 Conditionally Positive Promotional Terms

The following subsections describe positive promotional terms that may be used under certain conditions on drug product labels.

4.9.1 Market Share and Consumer Preference

Claims on drug product labels that include market share, sale, consumer and patient use/ choice, or preference must be supported by adequate studies conducted within the past year which should be kept on file by the manufacturer/sponsor. Although Health Canada does not review these label claims, where advertising disputes arise there are self-regulatory industry bodies that may deal with complaint resolution.

4.9.2 Clinically Proven or Tested

A. For a Product

The terms "clinically proven"or "clinically tested" can be used on drug product labelling provided:

- adequate clinical efficacy[13] data pertaining to the drug product has been reviewed and found acceptable by the Therapeutic Products Directorate; or
- it contains only one medicinal ingredient whose efficacy in a given dosage form and indication is well recognized and documented in the literature (e.g., Health Canada labelling standard or monograph for pharmaceutical drugs, or Category I ingredient- United States Federal Register).

An example would be dextromethorphan syrup in product X: "Product X is a clinically proven cough relief" or "clinically proven" would be acceptable on the label.

B. For an Ingredient

"Clinically proven" can be used on labelling for an ingredient when a drug product contains more than one medicinal ingredient, including one or more whose efficacy in a given dosage form and indication is well recognized and documented in the literature.

An example would be Product Y containing dextromethorphan and other ingredients that are not in any Health Canada labelling standard or monograph for pharmaceutical drugs, or in Category I, United States Federal Register. The statement "Dextromethorphan provides a clinically proven cough relief" would be acceptable, where as, the statement "Product Y is clinically proven" would not be acceptable.

Another example would be a combination drug product containing only dextromethorphan and pseudoephedrine hydrochloride, the benefits of both of which are documented in the literature: "Product Y provides clinically proven cough/nasal congestion relief" would be acceptable. The following statement would not be acceptable: "Product Y is a clinically proven cold relief" because the product is likely to alleviate only two cold symptoms, not the whole range of cold symptoms that may be present.

4.9.3 New

The word "new" may be used to describe a drug product that is marketed under its present brand name for the first time in Canada, or in a different version of an existing preparation (e.g., a new pharmaceutical form or strength). The use of the term "new" for more than one year of product sale is considered to be misleading.

If reformulating a drug product has changed one or more medicinal ingredients, manufacturers/sponsors are encouraged to indicate the modification by using a phrase such as "new formula" to alert the consumer. Similarly, when a dosage regimen has been modified, manufacturers/sponsors should indicate the change to the consumer.

4.9.4 Improved

For a drug product that has been modified in a manner that provides a significant therapeutic advantage over a previously marketed product of the same name (e.g., "oral powder formulation that is faster dissolving in water" or "smaller tablet that is easier to swallow"), it is acceptable to describe the drug product as "improved" for a period of one year from the date of introduction to market of this "improved" product. Manufacturers/sponsors should clearly explain the therapeutic advantage. This type of claim requires prior review and approval as part of the market authorization for the product.

In cases where the improvement refers to some non-therapeutic aspect of the formulation (e.g., taste, colour, texture), this should be specified. The manufacturer/sponsor is responsible for determining the acceptability and veracity of the claim. See also Section 4.8, "Cosmetic Claims."

4.9.5 Advanced

There are only a few drug products that can be considered "advanced" and labelled as such to the general public. Most drug products are part of a product class with similar product attributes, where it is difficult to identify any particular drug product as "advanced," compared to another in its class. To be considered "advanced," a drug product would require some new or added therapeutic benefit, which is clinically significant, meaningful, and easily identified by the consumer, compared to others in its therapeutic class.

The term "advanced" in a drug product name is acceptable in a therapeutic sense if the advanced product treats a wider range of symptoms or has an additional medicinal ingredient compared to a reference drug product in the same product line. Consistent with the extra strength policy (Section 4.9.6), the list of medicinal ingredients on the product label should clearly identify the additional ingredients responsible for use of the term "advanced."

In some cases, qualified claims concerning advanced non-therapeutic aspects (e.g., cosmetic aspects) may be acceptable if the non-therapeutic benefit is clearly explained. The manufacturer/sponsor is responsible for having data available on file to support these non-therapeutic claims.

4.9.6 Extra Strength

The use of terms such as "strong" or "extra strength" may be erroneous. Drug products are formulated to provide an amount of medicinal ingredient in an effective therapeutic range. The inclusion of a greater amount in a particular preparation or the marketing of more than one product to provide varying amounts of a medicinal ingredient within an acceptable range is undertaken at the manufacturer's/sponsor's discretion.

Use of this wording may imply that the drug product is therapeutically more effective, when in most cases there is no data to support a difference in product effectiveness within an acceptable dosage range and population.

The use of terms such as "regular strength" and "extra strength" are acceptable to describe drug products within a product line where various quantitative amounts of medicinal ingredient are provided. In most cases, the term "extra strength" can be used only if there is a regular strength reference product on the market containing the same medicinal ingredients. However, exceptions to this general interpretation are described in the following two subsections.

4.9.6.1 Single Ingredient Analgesics

Division 9 of the *Regulations* outlines standard dosage units for non-prescription analgesics (e.g., 325 mg acetaminophen (APAP) per dosage unit). Since dosage units for some analgesics are standardized by regulation, the use of the term "extra strength" to describe higher strength per dosage unit products is permitted. Health Canada considers that the term "extra strength" as useful information to the purchaser during product selection. Although there may not be a regular strength version of the same product by the same manufacturer/sponsor on the market, dosage units containing 500 mg of acetaminophen or acetylsalicylic acid (ASA) or more, are considered "extra strength" within the context of the established standards.

For single ingredient ASA or APAP products in strengths greater than 500 mg, terms other than extra strength should be used to distinguish them. For example, 500 mg, 650 mg, and 1000 mg acetaminophen products could be progressively described as "extra strength," "super strength," and "ultra strength" to differentiate these products.

In the case of children's dosage units, 160 mg acetaminophen products may be described as "extra strength" even in the absence of an 80 mg formulation in the product line.

4.9.6.2 Multiple Ingredient Drug Product

A multi-ingredient non-prescription drug product in a specific product line may claim "extra strength" in the brand name provided there is a regular strength drug product that contains the same ingredient or ingredients at the recognized "regular" therapeutic strength available on the Canadian market.

The specific extra strength ingredient or ingredients must be identified with a qualifier in the list of medicinal ingredients on the label (e.g., "extra strength acetaminophen for pain relief"). Ingredients clearly recognized to be extra strength such as 500 mg acetaminophen per single dose must declare "extra strength" as part of the product name. As noted in Section 4.9.6.1 of this guidance, a series of multiple ingredient products containing analgesics such as acetylsalicylic acid in 500 mg, 650 mg, and 1000 mg strengths should use different brand name descriptors such as "extra strength," "super strength," and "ultra strength" to differentiate the strengths in a multi-ingredient product line or product line extension (see Appendix A: Definitions).

For example, **Manufacturer A** submits a Drug Identification Number (DIN) application to market **Panacette Cough and Cold Tablets**:

- Acetaminophen 500 mg (analgesic/antipyretic)
- Phenylephrine hydrochloride 10 mg (nasal decongestant)
- Diphenhydramine hydrochloride 25 mg (antitussive)

If there is no regular strength drug product (325 mg acetaminophen) in Manufacturer A's product line, evidence can be provided to show that there are regular strength products with the same ingredients marketed by different manufacturers/sponsors available to the Canadian consumer. In this case, the acceptable drug product name would be **Extra Strength Panacette Cough and Cold Tablets**. The extra strength ingredient should be identified in the list of medicinal ingredients as follows:

Extra Strength Panacette Cough and Cold Tablets:

- Acetaminophen (extra strength) 500 mg (analgesic/antipyretic)
- Phenylephrine hydrochloride 10 mg (nasal decongestant)
- Diphenhydramine hydrochloride 25 mg (antitussive)

Drug products with undefined standard strengths will be evaluated on a case-by-case basis with data submitted to support the extra strength claim. The following lists of ingredients are in products that have defined standard strengths.

List of Ingredients in products that have defined standard strengths

Ingredient	Regular Strength	Extra or Ultra Strength
acetaminophen	325 mg	500 mg or 1000 mg
acetylsalicylic acid	325 mg	500 mg or 1000 mg
acetaminophen pediatric	80 mg	160 mg
dextromethorphan hydrobromide	10-20 mg	30 mg
pseudoephedrine hydrochloride	30 mg	60 mg
phenylephrine hydrochloride	10 mg	Not applicable
ibuprofen	200 mg	300 mg or 400 mg

4.9.7 Complete, Total

Reference to a therapeutic action as "complete" or "total" (e.g., complete relief) implies 100% efficacy, which is generally considered misleading for a drug product. No drug product works 100% of the time or is completely effective and to imply this is unacceptable, unless specific product data supports the claim.

However, the words "complete" or "total" have been accepted in the brand names of drug products to indicate that they treat several symptoms of a temporary condition (e.g., cough/cold products treating several symptoms of a cold) or have an additional medicinal ingredient than the reference product in the same product line.

Consistent with the use of "extra strength" (Section 4.9.6), the added ingredient or ingredients referred to or responsible for the use of the terms "complete" or "total" must be clearly identified as the medicinal ingredient(s) on the label to clearly differentiate this drug product from the reference product.

The naming of drug products in a product line extension should not create name confusion with respect to other products in the line. See Section 4.5, "Look-Alike, Sound-Alike Drug Product Names."

4.9.8 Plus

The use of the term "plus" in the brand name or as a label descriptor is acceptable in a drug product line that contains a reference product and where the "plus" product contains an additional amount of one or more ingredients or an added medicinal ingredient that provides an additional therapeutic benefit.

Consistent with the use of "extra strength" (Section 4.9.6), the added ingredient or ingredients referred to as "plus" must be clearly identified as the medicinal ingredient(s) on the drug product label (e.g., plus phenylephrine).

The term "plus" is also acceptable in the brand name of a product when an additional non-medicinal ingredient has been added to the formulation and is clearly identified on the label (e.g., Product X Antiperspirant plus Talc).

4.10 Potentially Misleading Promotional Terms

The following subsections describe potentially misleading promotional terms that should not be used on drug product labels unless specific data, rationale or circumstances support such a claim, or the addition of appropriate qualifying statements justify the wording.

4.10.1 Therapeutic Superlatives and Undue Emphasis

Descriptive wording and phrases to describe the activity, effects, attributes, formulation, or development of drug products should be chosen to ensure that the consumer can appreciate the actual situation. Terms such as "amazing," "astounding," "fantastic," "remarkable," "wonderful,", and other superlative terminology are considered inappropriate in drug product labelling.

Any undue emphasis, highlighting, or unbalanced presentation of one ingredient, attribute, claim, or feature of a multi-ingredient drug product at the expense of the other ingredients and attributes may be misleading as to the merit of the product. Examples may include highlighting:

- one ingredient in a multi-ingredient drug product;
- one indication in a drug product treating several symptoms;
- a secondary attribute (e.g., non-drowsy); and
- a non-therapeutic aspect at the expense of the therapeutic purpose (e.g., cleansing ability of a medicated shampoo).

Labels should represent the drug product identity and benefits equally and completely. For example, a combination cough/cold product containing acetaminophen, pseudoephedrine hydrochloride, and chlorpheniramine maleate should indicate at least one symptom treated by each of these ingredients.

There is no objection to adding inclusive statements on the main panel of the label (e.g., Brand X Cough Cold Product with Acetaminophen). Highlighting a non-medicinal ingredient is also acceptable if the non-therapeutic purpose is clearly identified (e.g., Brand X first aid cream with moisturizing aloe). See also Section 4.8, "Cosmetic Claims".

4.10.2 Maximum Strength

The term "maximum strength" may be misleading with respect to the composition and therapeutic merit of a drug product and is considered to be unacceptable in most cases. The term must be examined in the total context of the labelling.

This term is considered to be indefinable for most drug products and understood to mean the single or total daily dosage or both. Although regulatory limits may exist for the availability of certain non-prescription drugs (e.g., ibuprofen, benzoyl peroxide), there are no regulatory limits for a maximum dosage for prescription drugs. New scientific evidence may increase or decrease acceptable dosages depending on circumstances, and each drug product is evaluated on its own merits and the specific conditions indicated. The concept of absolute maximum limits for a drug product is difficult to maintain due to the variation of patient circumstance, product use, and the constantly changing scientific environment.

Moreover, the term "maximum strength" may create an erroneous impression of a greater (or maximum) therapeutic benefit to the consumer. This may encourage the consumer to believe that only a higher dose of medication can provide adequate relief of the symptoms, when often the regular strength product will provide sufficient relief. More accurate terms are preferred when describing a drug product in a product line containing various concentrations of an ingredient.

Where federal regulatory limits for non-prescription drug product availability exist, qualified statements accompanying the term maximum strength (e.g., "The highest level of benzoyl peroxide that you can buy without a prescription") have been accepted as statements of fact. The overall context of the use of such qualified statements would be evaluated on a case-by-case basis.

In addition to federal regulatory limits on the strength of some non-prescription drug products the provinces and territories may have further regulatory limits on the distribution of some drug products in their jurisdiction that may vary for each province and territory.

4.10.3 Concentrated, Potent, Strong

Drug product labels using descriptors such as "concentrated," "potent," or "strong" are often erroneous because drug products are formulated to provide an amount of medicinal ingredient within an effective therapeutic range. The inclusion of a greater amount of a drug in a particular preparation or the marketing of more than one product providing varying amounts of medicinal ingredient within an acceptable range is undertaken at the manufacturer's/sponsor's discretion and does not justify implying a concentrated drug product.

The use of such wording may imply that the drug product is therapeutically more effective when in most cases the data is not available to support a difference in effectiveness within a given acceptable dosage range and within a population. When data to support the descriptor has been reviewed and approved as part of the market authorization for the product, the manufacturer/sponsor can consider promoting products within a dosage range as being more effective.

However, there are situations where label descriptors such as "concentrate," "concentrated," or "highly concentrated," in conjunction with other directions (e.g., "must be diluted before use"), are very useful to alert consumers to the potential hazards of the product.

4.10.4 Unique, Special

The term "unique" is generally not considered acceptable on the labelling of drug products unless it refers to products that possess a unique therapeutic action or formulation of medicinal ingredients. There are a limited number of drug products that could be considered unique or exclusive in terms of action, effect, or formulation, particularly in classes of drugs where actions and attributes are quite similar.

The use of "unique" to describe a drug product is acceptable in the following situations:

- If a drug product is the only product on the market with particular medicinal ingredient(s) in that formulation, then the term "unique" could be an accurate description of that formulation, but not necessarily of the therapeutic class or effect of the product. If the difference is only in the concentration of the medicinal ingredient(s), the term "unique" would not be acceptable in this case.
- The terms "unique" and "special" should be reserved for those drug products that are singular or offer a distinct advantage to the consumer in terms of effect, lack of side effects, onset, duration, or other therapeutic benefit(s). The therapeutic benefit(s) should be specified in the labelling whenever this term is used. The use of "unique" would require justification and documentation to demonstrate the therapeutic advantage and would be evaluated on a case-by-case basis. The manufacturer/sponsor would be responsible for ensuring the continued suitability of the term as applied in the labelling of a particular drug product, especially in response to similar products entering the market.
- "Unique" and "special" may be acceptable when used to accurately describe the cosmetic or non-therapeutic aspects of a drug product. Phrases such as "contains a unique combination of moisturizing ingredients" and "with a unique fragrance" can be used to describe cosmetic elements or the use of descriptions (e.g., "in a unique package design") to describe non-therapeutic factors are acceptable provided the manufacturer/sponsor has the data on file to support these claims. See Section 4.8, "Cosmetic Claims."

4.10.5 Guarantee

No drug product can guarantee that it will be 100% effective. The use of this term without qualifying it is generally considered misleading and unacceptable. In some circumstances, manufacturers/sponsors may include an offer or guarantee of product quality (e.g., consistency, flavour, and colour) or other non-therapeutic benefit, if it is clearly worded.

4.10.6 Safe

As no drug product is completely safe and without potential for adverse effects, the unqualified term "safe" is considered to be generally misleading and unacceptable for drug product labels. However, in the context of providing adequate directions for use, the word "safe" may be part of the directions (e.g., "for safe use, do not exceed two tablets daily").

4.10.7 Healthy, Healthful

While drug products are intended to treat unhealthy conditions or to assist in maintaining good health, general unqualified descriptions of a drug product such as restoring general health or promoting healthful conditions are false. Manufacturers/sponsors should be more specific in identifying the therapeutic benefits of a particular drug.

4.10.8 Natural, Natural Action, Natural Source

The term "natural" to describe a drug product may imply some special benefit or added safety to consumers, which could be misleading as to the merit of the product. A drug product may be described as "natural" only

when it is sold in its original state without processing or refinement by humans. Where the original state of an ingredient is altered or changed, the use of the term "natural" in describing such a drug product would be false, misleading, or deceptive, and likely to create an erroneous impression regarding the character, composition, merit, or safety of the drug. This would be in violation of subsection 9(1) of the *Act*. Very few drug products are so devoid of processing to justify the description "natural."

Drug products of animal or vegetable origin and handled with minimal processing to retain most of the original constituents, may be described as "natural source." Although most of the products under this description may be natural health products subject to the *Natural Health Products Regulations*, combination products containing pharmaceutical and natural health products are considered pharmaceutical drug products; therefore, cannot be considered natural source due to the pharmaceutical content of the drug product. Because all drug products act by artificially stimulating or modifying the chemical functions of the body, the description of the pharmacological effect of a drug product as "natural" or "natural action" is false and not acceptable in drug product labelling.

4.10.9 Antioxidant

The unqualified term "antioxidant," when used in labelling, is considered to imply some vague therapeutic benefit of the drug product that is usually misleading, generally unsupported by the lack of available data, and should not be used. Manufacturers/sponsors wishing to use the term "antioxidant" should use adequate wording to make a more specific, therapeutically meaningful claim and provide substantiating data to support the claim.

In some narrow circumstances, manufacturers/sponsors may wish to refer to formulation ingredients which have an antioxidant function that preserves the drug product from degradation. This reference may be acceptable in terms of Good Manufacturing Practices, if it is clearly explained.

4.10.10 Free

Subsection 14(1) of the *Act* prohibits the distribution of any drug as a sample. Subsection 14(2) allows sampling to certain healthcare professionals and further *Regulations* apply to this activity. Although the *Act* and *Regulations*do not define a "sample." it has been defined in the Health Canada policy document *Labelling of Professional Samples of Drugs* as "a package of drug provided free of charge."

It is generally inappropriate to label any non-prescription drug product as "free." However, in a combination offer, such as a co-packaged non-prescription drug and non-drug product, the term "free" is acceptable with appropriate labelling (e.g., "Product Y free with the purchase of Product X"). Co-packaged products should be appropriately labelled, as outlined in Section 3.6.1, "Co-packaged Products."

4.10.11 False Representation

False representation is a presentation that contradicts current medical or scientific knowledge and is unsupported by clinically valid and statistically reliable data conforming to current standards. Such presentations may be considered in violation of section 9(1) of the *Act*. Due to the constant evolution of medical and scientific knowledge, claims that were once acceptable for a drug product may become invalid over time. Such claims include the use of outmoded therapeutic concepts (e.g., stomach acidifier). These claims may be significant in the labelling of older drug products that have not been recently updated. It is the manufacturer's/sponsor's responsibility to update labelling when label text is no longer valid.

4.10.12 Fortified, Enriched

The terms "fortified" and "enriched" are difficult to employ without creating an erroneous impression. In most cases this formulation change is limited to either the addition of an ingredient to a formulation or to an increase in concentration of an ingredient. Both these changes do not justify the use of the terms, where there is no proven therapeutic benefit for them. These terms may imply that the drug product is therapeutically better because it contains more of a certain ingredient, whereas the formulation remains

within an effective therapeutic range to accomplish the same effect and data is not available to show any differentiation in effect based on different strengths.

4.11 Negative Statements and Terminology

Drugs should be promoted in a positive fashion to provide the consumer with useful information. Negative statements may be derogatory, implying that another drug has a negative effect. A negative statement of this kind is considered to be misleading because it requires an interpretation of the implications of the statement by the consumer.

The following subsections describe different types of negative terminology.

4.11.1 Non-toxic and Non-narcotic

Negations such as "non-toxic," "non-poisonous," or "non-allergenic" create an erroneous impression regarding the safety of a drug product. No drug is completely harmless, especially if abused or misused.

"Non-narcotic" is also a misleading and deceptive term. Only those preparations sold under section 36 of the *Narcotic Control Regulations* are available to the general public without a prescription because their potential for abuse or misuse is limited. The term "non-narcotic" on a drug product label may negatively imply that other drugs in the same class are narcotizing, or have a potential for abuse, when this may not be the case. This is a misleading representation and is not acceptable.

Some consumers are concerned with the intake of certain non-medicinal ingredients in drug formulations (e.g., salt and sugar). Therefore, informative or qualifying statements regarding these ingredients may be acceptable. For additional information see Section 4.2, "Absence of Ingredients," and Section 4.3, "Absence of Side Effects."

4.11.2 Fear-inducing Text

Label text should not exaggerate the condition the drug product is meant to treat in such a way that will induce fear in the possible consequences of not treating the condition. It is not appropriate to suggest that the health of a consumer will suffer or that full health cannot be obtained unless a particular drug product is used. Most non-prescription products treat symptoms of self-limiting conditions, not the condition itself. Most conditions resolve on their own, with or without the use of medication.

It is also inappropriate to create fear of social embarrassment that may result from the consequences of a condition that may occur without the use of the medication (e.g., anti-diarrheal medications). Therefore, terms such as "dangerous," "violent," "harsh," "hazardous," and "acute" are generally unacceptable when describing symptoms.

However, in the consumer information documents for drugs containing an ingredient listed in the Prescription Drug List that treat serious conditions (e.g., cancer), the realities of the condition must be explained to fully inform the patient of the risks and benefits and this text may well be disturbing. A balance between fully informing the patient, and avoiding any unnecessary fear-inducing copy should be maintained for these products.

Similarly, for some non-prescription drug products that do treat the condition (e.g., vaginal antifungals) and where lack of treatment could have adverse consequences, a balance must be maintained between fully informing the patient of risks and benefits, and avoiding unnecessary fear-inducing text.

4.11.3 Acute, Severe, Chronic, Dangerous

Few conditions suitable for self-diagnosis and self-treatment in the non-prescription area would be considered acute, severe, chronic, or dangerous. In situations of a chronic or severe nature, the care and attention of a doctor or other healthcare professional is usually required. The use of these terms is generally considered misleading and unacceptable for non-prescription drug products. Similarly, such terms may not

be appropriate in the consumer labelling of prescription drugs, if considered to be unduly alarming or an exaggeration of the medical condition.

4.11.4 Need

Using the word "need" in labelling statements (e.g., "you need this drug") often conveys the erroneous impression that a particular drug product is essential to an individual's well-being. This term is inappropriate for most non-prescription drugs used to treat the symptoms and discomfort of self-limiting conditions that resolve on their own. Exceptions to this general statement for non-prescription drugs include vaginal antifungal preparations.

For prescription drug products, a doctor may decide a patient needs a particular drug product to treat a serious condition and wording in this context may be appropriate in the consumer information section of a prescription drug monograph (e.g., "Your doctor has determined that you need Product X to treat your blood infection Y"). Similarly, for certain non-prescription drug products (e.g., vaginal antifungals), a doctor's previous diagnosis is necessary for self-treatment of the same condition or symptoms and the term "need" could be considered for these product labels.

4.11.5 Tamper Resistant

The use of the term "tamper resistant" to describe the security feature of a drug product package should be avoided, as this language may tend to encourage or incite tampering behaviour in some individuals. More neutral language should be chosen to draw attention to the security feature (e.g., "security feature," "security band").

4.12 Product Cross-promotion

Cross-promotion of drug products with another drug, natural health product, medical device (e.g., toothpaste, electric toothbrush), cosmetic, food, or consumer good (e.g., drug product, movie) should be labelled using the following criteria:

1. There should be no direct or indirect safety concern, including inappropriate drug-drug, drug-natural health product, drug-cosmetic, or drug-food combinations.
2. There should be no direct or implied new therapeutic use for the cross-promoted products that may exceed the terms of market authorization for each of the individual products.
3. The cross-promoted drug products are not in violation of any *Regulations* applicable to any of the products.

See also Section 3.6.1, "Co-packaged Products."

4.13 Imagery, Symbols, Illustration

Using pictures, charts, graphs, statistics, and symbols in labelling can often be misleading as to the use, merit, and character of a drug product and should be avoided. Such representations include: pictures of the heart, EEG recordings, medical equipment, scientific reports, or medical lab test results. Often these additions to labelling may imply some therapeutic benefit that is unauthorized for that drug product (e.g., a picture of a heart on a package of acetylsalicylic acid tablets may imply some vague, undefined therapeutic benefit for the heart). All graphics that are considered to be therapeutically content-related, directly or indirectly implying any therapeutic attribute must be shown on the draft label included in the original drug submission (see Section 2.10, "Final Labels").

Note: Prescription products and those administered or obtained through a health professional have new requirements to file mock-ups of labels at the time of submission as of June 13, 2015. These mock-ups are not draft labels but should reflect the final label which, once approved, will be used to market these products.

5. Additional Considerations for Specific Product Types

5.1 New Drugs

All product monographs submitted in a new drug submissions filed in the new Product Monograph (PM) format, as outlined in the *Guidance for Industry: Product Monograph*, must include a consumer information/patient medication information section regardless of the type of product (e.g., prescription, non-prescription, or professional use only) and location of sale (e.g., for hospital use or professional use only).

For all new drug products in the new format, the consumer information/patient medication information document (i.e. the entire Part III of the PM) should be provided to the consumer/patient at the point of dispensing or sale.

For a prescription drug product, the consumer information/patient medication information is handed directly to the patient by the pharmacist or is already an integral part of the package given to the patient /consumer.

For a non-prescription drug product available in an open-selection area, the consumer information/patient medication information should be an integral part of the package purchased by the consumer.

In addition, labels for these products should indicate the availability and distribution of this consumer information/patient medication information, by wording such as:

- Pharmacist: Distribute/dispense consumer information/patient medication information for [prescription drug product];
- See enclosed consumer information/patient medication information for [prescription or non-prescription drug product]; or
- Doctor (Physician): Distribute consumer information/patient medication information with the professional samples of [prescription product].

Note: For new drugs in the old PM format where there is Information for the Consumer (i.e. Information for the Patient) section, the same label information as above is expected.

It is Health Canada's expectation that the manufacturer/sponsor supply the consumer information/patient medication information document to the pharmacist or doctor who will distribute this information to the patient/consumer.

Doctors are also responsible for distributing this information for samples given to patients.

5.2 Consumer Available Non-prescription Medicines

There are 3 basic sub-categories of non-prescription drugs:

a. those that may be sold freely to the general public without the intervention of a healthcare professional (e.g., consumer-available non-prescription drug products);
b. those that may not be sold to the general public without the intervention of a healthcare professional (e.g., nitroglycerin) in accordance with the provincial and territorial regulations; and
c. those that are sold directly to healthcare professionals and institutions and intended for professional use only (e.g., contrast media, some anesthetics).

For those in category a) consumer-available non-prescription drugs where there is no requirement for professional intervention, the wording of the product labelling is especially important to ensure safe and effective use. Special labelling considerations are outlined below in the following section for these products.

5.2.1 Labelling Standards and Monographs

Numerous labelling standards and monographs for general drug product classes have been developed for the common consumer-available non-prescription drug products and are available on the Health Canada website. These standards and monographs provide basic information on: acceptable indications, uses, medicinal ingredient identities, strengths, dosages, warnings, and precautions to help ensure the safe and effective use of products that fall within the standards. These standards and monographs should be consulted in conjunction with the *Act* and *Regulations*, and all other applicable Health Canada guidance and policy documents.

5.2.2 Directions for Use

Pursuant to section C.01.004 (1) (*c*) (iii) of the *Regulations,* drugs must carry adequate directions for use on the labels. Consumer-available non-prescription drugs products, intended for self-treatment by the general public, must carry sufficient information on the labels for an individual to use the medication properly without consulting a healthcare professional. Furthermore, the terminology used should be explicit and easy to interpret.

Adequate directions for use should include the following information:

- Indications for use;
- Dosage;
- Route of administration; and
- Warnings and precautions; and
- Storage conditions.

5.2.2.1 Indications for Use

In some cases, a pharmacological classification could suffice as an indication for use. However, such terminology has little meaning to the general public and specific indications are usually necessary. For example, the pharmacological classification of a drug product as an anti-emetic would be insufficient on a consumer-available non-prescription drug label; therefore, an additional indication such as "motion sickness" would be necessary.

Some indications for use may be evident in the trade name of the drug product, (e.g., "Brand X Sunscreen"). In contrast, "Brand Y Cough Syrup" would require further clarification indicating that it is an expectorant.

5.2.2.2 Dosage Directions

The dosage on consumer-available non-prescription drug product labels should state the number of tablets or capsules per dose, or the volume of product to be delivered (e.g., ml, teaspoon, tablespoon or where a calibrated dosing device should be used) and include the frequency of doses. Separate directions for adults and children should be provided and if the product is not recommended for children, the dosage should be clearly identified as "adult dose." Some drug products require a qualification on repeat doses (e.g., "may be repeated in X hours if required"). When applicable, maximum single and/or daily doses and duration of use for some conditions should be specified (e.g., "For treatment of pain: 650 mg every 4-6 hours as necessary with the recommended maximum dosage is 3 g daily. Self-medication should not exceed 10 days unless otherwise directed by your doctor.")

5.2.2.3 Routes of Administration

Labels should generally state the route of drug administration. Some consumer-available non-prescription drug products may have a brand name that includes the route of administration, or at least adequately implies it. Labels for tablets, capsules, and some liquids intended for oral administration may not require a separate statement, as the route of administration is often obvious. If the route of administration differs from the usual route associated with a pharmaceutical form, the label should specify the actual route (e.g., vaginal tablets, powder for inhalation, oral spray, or ophthalmic ointment).

Qualifying statements, such as "external use only," may be required if there is a possibility that the pharmaceutical form could indicate an alternate route of administration or cause confusion with other drug products (e.g., camphorated oil).

5.2.2.4 Warnings and Precautions

Frequently, a specific warning or precaution statement will be required for an individual drug product or product category. The warning may not, in itself, be a regulated statement, but it is considered an expression of adequate directions for use based on medical or pharmacological reasons.

Examples include: a) Cathartics are not to be used by children under six years of age b) Antihistamines that are known to cause drowsiness should be labelled so they are not to be used by individuals while operating machinery.

See also Section 3.5.4.3, "Warnings and Precautions."

5.3 Consumer-Available Non-prescription Medicines Subject to Narcotic Control Regulations

A particular subset of narcotic drug products can be supplied to consumers without a prescription as defined in section 36 of the *Narcotic Control Regulations*, which states:

36. (1) Subject to subsection (2), a pharmacist may, without a prescription, supply a preparation containing not more than 8 mg or its equivalent of codeine phosphate per tablet or per unit in other solid form or not more than 20 mg or its equivalent of codeine phosphate per 30 mL in a liquid preparation if:

a. the preparation contains:
    i. two additional medicinal ingredients other than a narcotic in a quantity of not less than the regular minimum single dose for one such ingredient or one-half the regular minimum single dose for each such ingredient, or
    ii. three additional medicinal ingredients other than a narcotic in a quantity of not less than the the regular minimum single dose for one such ingredient or one-third the regular minimum single dose for each such ingredient; and
b. there is legibly and conspicuously printed on the main panel of the label and on any outer container the full formula or true list of all active ingredients and a caution to the following effect:

    "This preparation contains codeine and should not be administered to children except on the advice of a physician or dentist."

Such drug products are usually pain medications containing combinations of ingredients such as acetaminophen or acetylsalicylic acid, caffeine, muscle relaxants, and codeine.

5.4 Prescribed and Parenteral Drugs

The general labelling requirements as described in Sections 2 and 3 of this guidance apply to prescribed and parenteral drug products, except as otherwise noted in this section. The language in the labelling of these drug products is usually written for healthcare professionals; however, the labelling should have sufficient information to promote safe and proper use of a drug product and well understood by all users.

5.4.1 Dosage

Unlike the labelling conventions for consumer-available non-prescription drug preparations, the dosage directions for prescription and parenteral preparations may often be expressed in terms of units of weight of drug per unit of body weight (e.g., mg/kg/day) or weight of drug per body surface area (e.g. mg/m2/day).

Although the pharmacological classification may replace specific indications on the drug labels, in cases where indications are specified, the dosage directions applicable to each indication or a dosage range encompassing all the indications should appear where possible. However, for complex prescription drug products with numerous indications and various dosage regimens (e.g., cancer drugs), providing complete dosage information on the package label may not be possible. In these cases, the prescription drug labelling may be abbreviated provided that there is direction to refer to the package insert or product monograph (e.g., "For dosage and administration: see package insert or product monograph").

When the label provides the dosage range, the specific dosage for each indication must be detailed in the prescribing information, package insert or product monograph.

5.4.2 Package Insert

The package insert for prescribed drug products is usually the prescribing information document described in Section 5.4.5. This is equivalent to Part I, Health Professional Information of the new Product Monograph format for new drugs. Both these documents are intended for use by a healthcare professional.

A package insert is not required to be included with these drug products. In these cases, manufacturers/sponsors should include a label statement such as "Product Monograph, package insert or prescribing Information available on request" to indicate that this information is available.

However, many manufacturers/sponsors choose to voluntarily include a package insert or Part I of the PM with the drug product as a convenience to the healthcare professional, particularly if special directions are required to prepare the product for dispensing (e.g., an injectable product requiring reconstitution).

If the package insert (Part I of the PM) is included in the package of a new drug, a separate consumer information/patient medication information document can be included in the insert or distributed separately.

If Part I (professional information) and Part III (consumer information/patient medication information) are included together in a package insert, then the label should indicate "See enclosed insert and consumer information/patient medication information." This variation in the label statement will alert the pharmacist dispensing the drug to provide the consumer information/patient medication information to the patient.

If Part III (consumer information/patient medication information) is not part of the package insert and is distributed separately, then the following two statements should appear on the label: "See package insert" and "Pharmacist: Dispense with consumer information/patient medication information (leaflet)."

Where multiple unit packages are supplied to the pharmacist (or doctor), it is expected that sufficient copies of the consumer information/patient medication information included in the packaging for distribution to the consumer/patient at the time of dispensing. It is Health Canada's expectation that the manufacturer/sponsor will supply the consumer information/patient medication information to the doctor or pharmacist who will distribute the information to the consumer/patient.

5.4.3 Parenteral Preparations

5.4.3.1 Common Name Parenterals

In addition to the general labelling requirements outlined in Sections 2 and 3, there is specific information that applies to parenteral drug products. In cases where no proper name exists for a single-ingredient parenteral preparation, the common name should be written in the following manner:

For liquids ready for injection:

"Substance X Injection"

(Substance X is to be shown as per Section 3.4.2, "Proper or Common Name").

For dry solids or concentrated liquids requiring dilution prior to administration:

"Substance X for Injection"

(Substance X is to be shown as per Section 3.4.2, "Proper or Common Name").

5.4.3.2 Products for Injection Requiring Dilution

If space is available on the label, concentrated liquid drug products meant for dilution before injection should bear a label warning stating "Concentrate - must be diluted before use." For small inner labels of these products, where space is limited, abbreviated statements such as "dilute before use" may be used.

For other injectable drug products such as powdered or special products (e.g., products stored in a droplet of oil under nitrogen in an ampoule) that must be reconstituted or diluted before use, the label warning can state "Reconstitute (dilute) before use."

For special labelling of pharmacy bulk vials, see Section 5.4.3.8.

5.4.3.3 Declaration of Medicinal Ingredients

A. Liquid preparations

- For small volume parenterals, the quantity of each medicinal ingredient should be declared per millilitre (e.g., 5 mg/mL), the total volume (e.g., 4 mL), and the total quantity per total volume (e.g., 20 mg/4 mL) in each container.
- For large volume parenterals, declarations of each medicinal ingredient in percentage or weight per 100 mL (e.g., 1g /100 mL, or 1% w/v) would be acceptable according to existing practices, as well as total volume (e.g., 250 mL) and the total quantity per total volume (e.g., 2.5 g/250 mL) for each container.

B. Preparations intended for reconstitution

- The quantity of each medicinal ingredient per container should be declared.
- The method of reconstitution, including the name and quantity of the diluent to be used, and the resulting concentration, should be declared.
- The volume of liquid that can be withdrawn for administration after reconstitution should also be declared.

The potency of medicinal ingredients may be declared in terms of the total compound or the active moiety, provided that the whole compound is identified by name. The dosage recommendations should follow the chosen method of potency declaration. For a drug product available in different potencies, the method of declaration should be identical for all potencies.

For further optional information on the labelling of parenteral preparations refer to Appendix C.

5.4.3.4 Declaration of Non-medicinal Ingredients

The *United States Pharmacopoeia* requires that the labelling of parenteral preparations list the names and quantities of all ingredients except ingredients added to adjust the pH or to make a solution isotonic, which may be declared by name with a statement of their effect. For drug products that are not declaring the USP standard, sponsors should provide the qualitative declarations of the complete formulation of parenteral preparations in all cases. This information is useful in promoting safe and proper use of these drug products.

5.4.3.5 Declaration of Preservatives

For the purposes of section C.01.004 (2) (*b*) of the *Regulations*, which requires the quantitative declaration of preservatives used in parenteral preparations, the term "preservatives" refers only to antimicrobial agents.

5.4.3.6 General Directions for Use

In addition to the regulatory requirements for the labelling of injectable products which includes the declaration of preservatives, labelling should also state the following information:

A. Label Only

- The route of administration (e.g., intravenous, subcutaneous);
- If no preservatives are present, wording such as "Single use. Discard unused portion";
- If preservatives are present, wording such as "multiple use" as well as wording to explain duration, the conditions of use and the storage after first puncture of the multiple use product (e.g., "use within X hours of first puncture when stored at Y-ZEC"); and
- If dilution is required, the directions for performing the dilution.

B. Label or Insert

- Directions to examine the solution for drug product integrity before use such as "mixture (solution) should be inspected visually for clarity, particulate matter, precipitation, discolouration, and leakage prior to administration whenever solution and container permit." Optional wording could include "Do not use product if mixture (solution) shows haziness, particulate matter, discolouration, or leakage"; and
- Any special directions for the preparation, reconstitution, administration, volume, rate and timing of infusion, mixing and incompatibilities with other medications, period of use after reconstitution, storage, special handling, and disposal.

5.4.3.7 Parenteral Salts, Salt/Sugar, Electrolytes, Parenteral Nutrition

For all parenteral electrolyte salts, or salt/sugar combinations, the quantitative declaration for each ingredient in terms of weight (per volume or per container) and final concentration after dilution, must be shown on the labels. In addition, special labelling may be required to show the total osmolar concentration of the final formulation. The label may also require the declaration of the number of milliequivalents per total volume (mEq/volume) for each salt/electrolyte. Osmolarity is usually expressed in terms of mOsmol/L, or for volumes less than 100 mL, in terms of mOsmol/100 mL. The following table show several examples.

Table 5.1: Additional Labelling Requirements for Parenteral Salts and Salt/Sugar Combinations

Salt, salt/sugar combination	Total Osmolarity mOsmol/Litre, or mOsmol/100mL	Declaration (mEq/volume)
Sodium chloride injection	Yes	No
Sodium chloride and dextrose injection	Yes	No
Potassium chloride in dextrose injection	Yes	Yes, in terms of potassium and chloride
Potassium chloride in dextrose and sodium chloride injection	Yes	Yes, in terms of potassium, sodium, chloride
Multiple electrolytes in dextrose injection	Yes	Yes, for all electrolytes, which may include, but not limited to and in terms of : sodium, potassium, magnesium, chloride, calcium, acetate, gluconate, phosphate, lactate, ammonium, sulfate

5.4.3.7.1 Parenteral Nutrition products

For parenteral nutrition drug products that have been assigned DINs, including those providing electrolytes and calories by sugars and/or by fat emulsions, the same requirements of section 5.4.3.7 are applicable as well as the requirement to include the declaration of osmolarity. In addition, the caloric content provided per unit volume should be declared (e.g., kcal/mL) and the maximum daily limit of the product to be administered intravenously (e.g., 2 g fat/kg body weight/day).

5.4.3.8 Pharmacy Bulk Vials

Pharmacy bulk vials are large volume vials containing multiple doses and are intended for a pharmacy admixture program to create infusion mixtures or transfer to empty sterile syringes. These vials are not meant for direct injection. The closure to each vial is meant to be penetrated one time only with a sterile transfer device.

The following additional labelling is required for pharmacy bulk vials:

To be shown prominently, preferably on the main panel of the label:

- "Pharmacy Bulk Package (Vial) - not for direct infusion.";
- "Single puncture - multiple dispensing."

On any panel:

- "For use in pharmacy (hospital) admixture program only."

5.4.4 Prescribed Drugs containing an ingredient not Controlled by Federal Schedules or the Prescription Drug List

In accordance with Federal Legislation, there are some unscheduled non-prescription drug products that do not require a prescription as a condition of sale but are generally prescribed by a medical practitioner. These drug products can be easily accessible by consumers for certain medical conditions or for emergency use (e.g., nitroglycerin, insulin). Pursuant to provincial or territorial regulations, these drugs are kept behind the counter in pharmacies and must be distributed by a pharmacy healthcare professional (e.g., pharmacist). They should not be advertised, labelled, or recommended to the general public for self-medication (e.g., drugs where the dosage exceeds the limits of section C.01.021 and drugs intended for the treatment of diseases listed in Schedule A of the *Act*).

Schedule A diseases should not be included in the labelling of drug products that are available to the general public, unless the information is required for warnings and precautions or they have been authorized as preventative claims for some non-presciption drugs (see Section 2.7, "Schedule A Claims").

In cases where a product is intended for a Schedule A disease and there is no appropriate pharmacological classification or indication other than the one that would refer to such disease, no pharmacological classification or indication should appear on the label (section 3(2) of the *Act*). Prescribing information that includes the indication must therefore be made available for physicians and pharmacists, and the label should state the availability of this document. The label should also include a statement indicating that the drug product is to be used only on a physician's advice.

Many of the drug products in the categories covered by this section which are not new drugs require that the directions for use be detailed in a document called "prescribing information" (see Section 5.4.5 of this Guidance Document). However, there are some drugs (e.g., new drugs) that require a product monograph if they have received market authorization through the issuance of a Notice of Compliance (e.g., Plan B).

Note: As of June 13, 2015, there are new regulatory requirements for prescription products and those administered or obtained through a health professional. These products are required to include contact information on their labels to report harms (see section 2.1.2 of this guide) and are required to submit mock-

ups of labels with their submissions, instead of draft text (see section 2.10). While the regulations are not retroactive in application, sponsors are expected to bring their labels into compliance with the new regulations at the first submission after June 13, 2015 which requires a label change.

5.4.4.1 Oral Use Salts

Drug products that contain salts for oral use (e.g., potassium chloride for oral solution) or combinations of salts for oral use (e.g., oral rehydration solutions, electrolyte replenishers) should include the quantitative declaration in terms of weight of each medicinal ingredient per container, and weight per final volume after dilution. In addition, the quantity should also be expressed in milliequivalents per unit of final volume for each element (ion).

5.4.5 Prescribing Information

The prescribing information (i.e. professional information) for new drug products not conforming to the new Product Monograph format or for products not subject to Division 8 of the *Regulations* should contain at least the following:

- Brand name, if applicable;
- Proper or common name, and potency or quantitative list of the medicinal ingredients;
- Indications; this section must clearly indicate the function of the drug product in either the treatment, prevention, or diagnosis of a recognized disease entity or a significant manifestation of disease, or in the relief of symptoms associated with a recognized disease, condition, or syndrome, or as an adjunct in the treatment of some condition;
- Contraindications, precautions, warnings, and adverse effects, drug/drug interactions, and drug/food interactions;
- Dosage and administration instructions for each indication and age group or other patient categories, as applicable;
- Mode of reconstitution and storage, if applicable;
- Symptoms and treatment of overdosage;
- Preparations available;
- Identification of manufacturer/sponsor; and
- Date of preparation or document revision.

Manufacturers/sponsors can use the above format when updating old prescribing information documents, creating new prescribing information documents where none previously existed, or when this information does not have to be incorporated into the new Product Monograph format. Alternatively, it is recommended that the new format as outlined for Part I of the *Guidance for Industry: Product Monograph* is followed where possible.

5.5 Notice of Compliance with Conditions

Health Canada's *Notice of Compliance with Conditions (NOC/c) Guidance* describes New Drug Submissions or Supplemental New Drug Submissions for serious, life-threatening, or severely debilitating disease for which promising evidence of clinical effectiveness exists. Special labelling is required to clearly identify and highlight these products and the tentative nature of their approval. See Appendix B.

5.6 Professional Use Products

A further category of federally unscheduled (i.e., prescribed non-prescription) drug products is the "professional use only" products. These products are available to and intended for use by a healthcare professional and are distributed to hospitals, clinics or directly to physicians, dentists, and other healthcare professionals.

Professional use only drug products include:

- contrast media for magnetic resonance imaging (MRI) and other imaging agents;
- dental-use hemostat agents to stop bleeding in dental surgery;
- dyes for revealing dental plaque;
- dental antiseptic solutions for administration by dental professionals; and,
- dialysis solutions.

As most of these products are distributed only to healthcare professionals, and have been used by these professions for a long time, the labelling requirements for some of these drug products may be minimal (except contrast media) and a prescribing information document may not be needed. To distinguish these products from similar consumer-available non-prescription drug products (e.g., fluoride products), and to avoid unintentional diversion to consumer markets, the labelling should state "For professional use only." Note: After June 13, 2015, these products are subject to new requirements for their labels, which include contact information to report harms (see section 2.1.2 of this guidance document), legibility of information (section 2.3), the submission of mock-ups of labels and packages instead of draft text (section 2.10) and brand name assessment of the labels (section 4.5).

Appendix A: Definitions

Adequate Directions for Use: "means information necessary for the proper and recommended use of the drug, including cautionary and warning statements" (*Regulations*, section C.01.004 (1) (*c*) (iii)).

Brand Name: "means, with reference to a drug, the name, whether or not including the name of any manufacturer, corporation, partnership, or individual, in English or French,

a. that is assigned to the drug by its manufacturer;
b. under which the drug is sold or advertised; and
c. that is used to distinguish the drug" (*Regulations*, section C.01.001).

Child Resistant Package: "means a package that meets the requirements of subsection (2)" (*Regulations*, section C.01.001).

Close Proximity: "means, with reference to the common name, immediately adjacent to the common name without any intervening printed, written or graphic matter" (*Regulations*, section B.01.001).

Common Name: "means, with reference to a drug, the name in English or French by which the drug is

a. commonly known, and
b. designated in scientific or technical journals, other than the publications referred to in Schedule B to the *Act*" (*Regulations*, section C.01.001) See section 3.4.2 of this guidance.

Drug: "includes any substance or mixture of substances manufactured, sold or represented for use in

a. the diagnosis, treatment, mitigation or prevention of a disease, disorder or abnormal physical state, or its symptoms, in human beings or animals,
b. restoring, correcting or modifying organic function in human beings or animals, or
c. disinfection in premises in which food is manufactured, prepared or kept" (Section 2 of the *Act*).

Dosage Form: A drug product that has been processed to the point where it is now in form which may be administered in individual doses.[14]

Drug in Dosage Form: "means a drug in a form in which it is ready for use by the consumer without requiring any further manufacturing" (*Regulations*, subsection C.01.005 (3)).

Expiration Date: "means the earlier of

a. the date, expressed at minimum as a year and month, up to and including which a drug maintains its labelled potency, purity and physical characteristics, and
b. the date, expressed at a minimum as a year and month, after which the manufacturer recommends that the drug not be used" (*Regulations*, section C.01.001). See Section 3.5.3 of this guidance.

Immediate Container: "means the receptacle that is in direct contact with a drug" (*Regulations*, section C.01.001).

Inner Label: "means the label on or affixed to an immediate container of a food or drug" (*Regulations*, section A.01.010).

Internal Use: "means ingestion by mouth or application for systemic effect to any part of the body in which the drug comes into contact with mucous membrane" (*Regulations*, section C.01.001).

Label: "includes any legend, word or mark attached to, included in, belonging to or accompanying any food, drug, cosmetic, device or package" (Section 2 of the *Act*).

Lot Number: "means any combination of letters, figures, or both, by which any food or drug can be traced in manufacture and identified in distribution" (*Regulations*, section A.01.010).

Main Panel: see Principal Display Panel.

Manufacturer or Distributor: "means a person, including an association or partnership, who under their own name, or under a trade, design or word mark, trade name or other name, word or mark controlled by them, sells a food or drug" (*Regulations*, section A.01.010). See Section 3.5.1 of this guidance.

Microgram: one-millionth of a gram.

Mock-Up: A full colour, actual size copy of the labels and a colour representation (i.e. photograph) of the packages intended to be used for the sale of the drug, including all presentation/design elements, proposed graphics, fonts, colours and text (with a place holder for expiry date, DIN, and lot number).

Net Amount: "in addition to the requirements of subsection (1), the outer label of a drug shall show (a) the net amount of the drug in the container in terms of weight, measure or number...." (*Regulations*, section C.01.004 (2) (*a*)).

New Drug: "means

a. a drug that contains or consists of a substance, whether as an active or inactive ingredient, carrier, coating, excipient, menstruum or other component, that has not been sold as a drug in Canada for sufficient time and in sufficient quantity to establish in Canada the safety and effectiveness of that substance for use as a drug;
b. a drug that is a combination of two or more drugs, with or without other ingredients, and that has not been sold in combination or in the proportion in which those drugs are combined in that drug, for sufficient time and in sufficient quantity to establish in Canada the safety and effectiveness of that combination and proportion for use as a drug; or
c. a drug, with respect to which the manufacturer prescribes, recommends, proposes or claims a use as a drug, or a condition of use as a drug, including dosage, route of administration, or duration of action and that has not been sold for that use or condition of use in Canada, for sufficient time and in sufficient quantity to establish in Canada the safety and effectiveness of that use or condition of use of that drug" (*Regulations*, section C.08.001).

Non-prescription Drug:a drug containing ingredients not listed on the Prescription Drug List and available without a prescription. This includes drugs that

a. may be sold to the general public (consumer-available non-prescription drug products) without the intervention of a healthcare professional (e. g. acetylsalicylic acid (ASA));
b. may not be sold to the general public without the intervention of a healthcare professional, usually a pharmacist (e.g., nitroglycerin, insulin, injectable epinephrine for anti-allergic purposes); and
c. are sold directly to healthcare professionals and intended for professional use. (e.g., contrast media, anesthetics).

Official Drug: "means any drug

a. for which a standard is provided in these *Regulations*, or
b. for which no standard is provided in these *Regulations* but for which a standard is provided in any of the publications mentioned in Schedule B to the *Act*" (*Regulations*, section C.01.001).

Outer Label: "means the label on or affixed to the outside of a package of a food or drug" (*Regulations*, section A.01.010).

Parenteral Use: "means administration of a drug by means of a hypodermic syringe, needle, or other instrument through or into the skin or mucous membrane" (*Regulations*, section C.01.001).

Prescribed: "means prescribed by the *Regulations*" (Section 2 of the *Act*).

Principal Display Panel: "has the same meaning as in the *Consumer Packaging and Labelling Regulations".* (*Regulations*, section A.01.010) (CPLR). The *Consumer Packaging and Labelling Regulations* (CPLR) state:

"Principal display panel means

a. in the case of a container that is mounted on a display card, that part of the label applied to all or part of the principal display surface of the container or to all or part of the side of the display card that is displayed or visible under normal or customary conditions of sale or use or to both such parts of the container and the display card,
b. in the case of an ornamental container, that part of the label applied to all or part of the bottom of the container or to all or part of the principal display surface or to all or part of a tag that is attached to the container, and
c. in the case of all other containers, that part of the label applied to all or part of the principal display surface."

The alternate term, *main panel* has the same meaning as "principal display panel".

Product Class: for the purpose of this guidance, a product class consists of drug products indicated for the same condition or range of symptoms, and sold under similar regulatory requirements.

Product Line or Product Line Extension: two or more drug products sharing a brand name, part of a brand name, or common identifier as part of the brand or product name that contains additional medicinal ingredients or different strengths and is intended to expand the conditions of use of the initial product. Product line extensions should not create name confusion with respect to other products in the line. See Section 4.5, "Look-alike, Sound-alike Drug Product Names of this guidance."

Proper Name: "means, with reference to a drug, the name in English or French

a. assigned to the drug in section C.01.002,
b. that appears in bold-face type for the drug in these *Regulations* and, where the drug is dispensed in a form other than that described in this Part, the name of the dispensing form,
c. specified in the Canadian licence in the case of drugs included in Schedule C or Schedule D to the *Act*, or
d. assigned to any of the publications mentioned in Schedule B to the *Act* in the case of drugs not included in section (*a*), (*b*) or (*c*)" (*Regulations*, section C.01.001).

Security Package: "means a package having a security feature that provides reasonable assurance to consumers that the package has not been opened prior to purchase" (*Regulations*, section A.01.010). See Section 3.6.4 of this guidance.

Standard: a monograph for a drug substance (as the medicinal ingredient) or the drug product (as the finished dosage form) that lists specifications relating to nomenclature, identity, purity, potency, quality, physical properties, tests, assays, packaging, labelling, and storage requirements. See Section 3.4.3 of this guidance.

Teaspoon: "means, for the purpose of calculation of dosage, a volume of 5 cubic centimetres" (*Regulations*, section C.01.001).

Tablespoon: a volume of 15 cubic centimetres (15 cm^3).

Appendix B: Applicable Health Canada Guidance Documents and Policies

Health Canada Guidance Documents

The following guidance documents are available on the Health Canada Website.

Frequently Asked Questions - Guidance Document for Industry- Review of Drug Brand Names

Guidance Document: Questions and Answers: Plain Language Labelling Regulations

Guidance Document: Schedule A and Section 3 to the Food and Drugs Act.

Good Manufacturing Practices (GMP) Guidelines - 2009 Edition, Version 2 (GUI-001)

Guidance Document: Basic Product Monograph Information for Nonsteroidal Anti-Inflammatory Drugs (NSAIDs).

Guidance Document: Disinfectant Drugs.

Guidance for Industry: Post Drug Identification Number (DIN) Changes

Guidance for Industry : Post Notice of Compliance (NOC) Changes

Guidance for Industry: Review of Drug Brand Names

Guidance for Industry: Management of Drug Submissions.

Guidance for Industry: Product Monograph.

Guidance for Industry: Product Monographs of Non-Contraceptive Estrogen/Progestin-Containing Products.

Guidelines for Temperature Control of Drug Products during Storage and Transportation (GUIDE-0069).

Guideline on Preparation of DIN Submissions

Non-medicinal Ingredient Nomenclature.

Guidance Document: Notice of Compliance with Conditions (NOC/c)

Therapeutic Comparative Advertising: Directive and Guidance Document

Health Canada Policies

The following policies are available on the Health Canada website.

Absence of Ingredient Statements for Non-prescription Drugs

Assignment of Drug Identification Numbers (DIN) According to Product Name

Changes in Manufacturer's Name and/or Product Name

Drug Identification Number: A Brand Name Product with Different Fragrances, Flavours or Colours

Herbs used as Non-medicinal Ingredients in Non-prescription Drugs for Human Use

Labelling of Professional Samples of Drugs

Labelling of Special Containers.

Principles for Claims Relating to Comparison of Non-therapeutic Aspects of Non-prescription Drug Products

The Distinction between Advertising and Other Activities

Other Applicable Legislation

Benzodiazepines and Other Targeted Substances Regulations

Controlled Drugs and Substances Act

Narcotic Control Regulations

Weights and Measures Act, 1985. (Administered by Measurement Canada, an agency of Industry Canada)

Regulations Amending the Food and Drug Regulations (743- Non-medicinal ingredients) Canada Gazette, Part II, vol. 44, no. 11, May 26, 2010, SOR.2010-105, May 13, 2010

Appendix C: Third-party Guidance Documents

The following is a list of further labelling guidance documents from third parties or other countries that sponsors may wish to consider when creating effective labelling. Health Canada does not endorse the following documents and does not necessarily agree with their entire contents. They are presented as sources of additional, useful information should the sponsor wish to further improve labelling, providing these improvements do not conflict with the *Regulations* and related guidance documents.

Good Medicine for Seniors: Guidelines for Plain Language and Good Design in Prescription Medication. 2002, ISBN: 1-894324-23-4, Canadian Public Health Association, <www.cpha.ca>.

Guidelines for Cosmetic Advertising and Labelling Claims. February 2006. Health Canada/Advertising Standards Canada. HC Pub: 4285, Cat H128-1/06-453, ISBN 0-662-49001-0 Available on the Advertising Standards Canada Website at: <www.adstandards.com/en/clearance/cosmetics/guidelinesforcosmeticadvertising.aspx>.

Guidelines for Drug Packaging and Labelling for Manufacturers. 2001. Canadian Society of Hospital Pharmacists, <www.cshp.ca>.

Guideline on the Readability of the Labelling and Package Leaflet of Medicinal Products for Human Use. 12 January 2009. European Commission, Directorate-General III Industry.

Institute of Safe Medication Practices (ISMP), <www.ismp.org>.

a. *ISPM's List of Confused Drug Names*
b. *ISMP List of Error-Prone Abbreviations, Symbols, and Dose Designations*
c. *Principles of Designing a Medication Label for Intravenous Piggyback Medication for Patient Specific, Inpatient Use*.
d. Eliminate use of dangerous abbreviations, symbols and dose designations ISMP Canada Safety Bulletin, 2006, vol.6, issue 4.
e. *Canadian Pharmaceutical Bar Coding Project*
f. *ISMP Canada, Jan. 15, 2010, www.ismp-canada.org/barcoding.index.htm*

Labelling Code of Practice: Designing Usable Non-prescription Medicine Labels for Consumers. 2004, Communication Research Institute of Australia (CRIA), <www.communication.org.au>.

Labelling of Drug Ampoules, Vials and Prefilled Syringes. CAN/CSA-Z264.2-99. Canadian Standards Association, <www.csa.ca>.

Part 201 - Labelling: Subpart C - Labelling Requirements for Over-the-Counter Drugs. Section 201.66 Format and Content Requirements for Over-the-Counter (OTC) Drug Product Labelling. Code of Federal Regulations, Title 21, Volume 4. Revised as of 1 April 2008, 21CFR201.66. (US).

Part 201 - Labelling: Subpart B - Labelling Requirements for Prescription Drugs and/or Insulin. Section 201.56 Requirements on Content and Format of Labelling for Human Prescription Drug and Biological Products. Code of Federal Regulations, Title 21, Volume 4, Revised as of 1 April 2008. 21CFR201.56 (US).

USP Nomenclature Policy: Monograph Naming Policy for Salt Drug Substances in Drug Products and Compounded Preparations.
USP Pharmacopeial Convention
www.usp.org/USPNF/notices.general Chapter1121.html

Footnotes

1. The labelling of small containers is exempt from many of these requirements. See sections 3.6.2 and 3.6.3 of this guidance document for more information and exceptions.
2. The labelling of small containers is exempt from many of these requirements. See sections 3.6.2 and 3.6.3 of this guidance document for more information and exceptions. See section 3.5.6 regarding regulatory changes in the declaration of non-medicinal ingredients on the label, effective May 13, 2012.
3. With the exception of submissions for which there is no previously approved Product Monograph (i.e. New Drug Submissions). These types of submissions are required to file the second language versions of the Product Monograph and Package Insert no later than 15 days after the submission is accepted into review. For more information, please consult the *Guidance Document: Questions and Answers on Plain Language Labelling Regulations* at section 5.
4. Division 1 drug: a drug that was submitted to Health Canada as a Drug Identification Number application (DINA) and approved pursuant to the requirements of Division 1 in Part C of the *Food and Drug Regulations*.
5. In Canada, Aspirin is a registered trademark and a brand name.
6. There are exceptions for small containers as outlined in section 3.6.3.
7. There are exceptions for small containers as outlined in section 3.6.3.
8. Optional for professionally administered drug products.
9. There are exceptions for small containers as outlined in section 3.6.3.
10. Refer to Section 5.4, "Prescribed and Parenteral Drugs," for further information.
11. Division 1 drug: a drug that was submitted to Health Canada as a Drug Identification Number application (DINA) and approved pursuant to the requirements of Division 1 in Part C of the *Food and Drug Regulations*.
12. Division 1 drug: a drug that was submitted to Health Canada as a Drug Identification Number application (DINA) and approved pursuant to the requirements of Division 1 in Part C of the *Food and Drug Regulations*.
13. Adequate clinical efficacy data is defined as statistically significant clinical efficacy data, obtained from a minimum of two separate, well controlled studies that reflect a representative population and are of sufficient duration. Survey data and anecdotal results are unacceptable for this purpose. Under some special circumstances, a large single study may be considered sufficient; however, the sponsor should contact Health Canada for guidance beforehand on this issue.
14. From Good Manufacturing Practices (GMP) Guidelines- see Appendix B