

Plain Language Labeling (PLL)

By Mary Speagle, RAC

Drug labels are one of the primary methods for communicating important information to health professionals, patients and consumers. For the health professional, labels support appropriate prescribing, dispensing, administration and patient counseling. For the patient, they relay important messages and reinforce healthcare professional counseling. For consumers, labels support proper drug selection and use where there may be limited to no health professional interaction.

Plain Language Labelling (PLL) Regulations

Crowded and confusing drug labels, unclear instructions and similarities between packages and names contribute to medication errors. In response to the high rate of medication errors observed in the health system and recognizing the role of the label and Health Canada oversight both pre- and postmarket, significant work was undertaken to identify methods to improve drug label clarity and accessibility. Following Health Canada consultations dating back to 2011, the *Food and Drug Regulations (FDR)* were amended to better reflect current knowledge about medication use and ways to minimize potential confusion arising from labels, packages and names. These amendments also aimed to align with international best practices.

The 2014 *Regulations Amending the Food and Drug Regulations (Labelling, Packaging and Brand Names of Drugs for Human Use)* are commonly referred to as the *Plain Language Labelling (PLL) Regulations*. These regulations are intended to improve the safe use of prescription and nonprescription pharmaceutical drugs, biologics and radiopharmaceuticals by making labels easier for the target audience to read and understand and to ensure label format or presentation does not impede comprehension.

Under the *PLL Regulations*, health product sponsors are obliged to:

- provide information in plain language
- assess their health products' names to avoid confusion

- submit label and package mock-ups for review
- indicate on the product label how to report harms
- provide information in an easy-to-read and standardized format
- for nonprescription drugs, provide a Canadian Drug Facts Table (CDFT)

The *PLL Regulations* were implemented using a phased-in approach that came into force 13 June 2015 for prescription drugs, biologic drugs, radiopharmaceuticals and drugs administered through a health professional. PLL came into force for nonprescription drugs on 13 June 2017.

These *FDR* amendments are supported by such nonregulatory instruments as guidance, best practices and collaboration with other stakeholders who play a role in developing and disseminating important safety information. For prescription drugs and those administered under a healthcare professional's supervision, two key guidance documents address *PLL* requirements: *Questions and Answers: Plain Language Labelling Regulations for Prescription Drugs* and *Good Label and Package Practices Guide for Prescription Drugs*.

For nonprescription drugs, similar *Questions and Answers* and *Good Label and Package Practices Guides* apply. Several additional guidances address some unique nonprescription drug aspects such as the CDFT. General *PLL* information for nonprescription drugs is presented below with a more detailed discussion in Chapter 9.

Good Label and Package Practices Guides

Good Label and Package Practices Guides (GLPPGs) have been developed to support safe, clear and effective label and package design. Recommendations address regulatory requirements as well as complementary information important to proper product identification, selection and use. Location of use (e.g., hospital,

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long-term care facility, patient's home), location of storage, types of supporting tools and technologies (i.e., barcoding, dose organizers and dispensers, medication administration records) and lighting level all factor into environment of use. One *GLPPG* is for prescription pharmaceuticals, biologics, radiopharmaceuticals and drugs permitted to be sold without a prescription but obtained or administered only under healthcare professional direction (i.e., insulin, nitroglycerin, epinephrine for allergic purposes). The other is for nonprescription drugs, natural health products and contact lens disinfectants. Basic considerations for good label design are applicable to both prescription and nonprescription drugs.

Presentation

A.01.017 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 on it
 - 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).

Label Design and Layout

When designing labels, standardization can reduce errors by reinforcing pattern recognition; however, there needs to be a balance between label similarities and differences to avoid look-alike issues. In planning label design, general aspects for consideration include any prior experience in other markets, product-use process maps, consideration of other products that may be used simultaneously with the product of interest, experience in other markets, user testing and other methods, mock-up preparation and a continuous improvement approach.

Factors to consider include type style, weight and size; use of TALL man lettering (writing groups in capital letters) text alignment; contrast and spacing; color; use of white space; proximity and compatibility of information (all information relevant to a common task or mental operation should be displayed close together); logos; trade dress and branding; presentation of bilingual text; use of abbreviations, symbols and dose designations (these should be minimized); and permanence.

Label Information

The principal display panel is the first user-label interface and an important factor in product identification and selection. Eight elements have been identified by an expert advisory panel as the key pieces of information to include on a health product label's principal display panel to support appropriate selection and use. These elements complement regulatory recommendations and align with national and international standards and safety literature. They do not incorporate all the elements required by regulation or guidance.

The eight key elements are:

- health product brand name
- health product nonproprietary name (proper or common name)
- strength, with or without total amount per total volume
- dosage form
- route of administration (other than for oral solids, such as tablets)
- critical warnings, as relevant
- population, as relevant (e.g., pediatric)
- storage instructions, as relevant

Depending on the product specifics and environment of use, one or more of the key elements may have greater importance.

The *GLPPGs* provide detailed guidance for specific elements such as expression of strength, critical warnings, expiry date, lot or batch number and barcoding.

The Q&A documents provide expanded guidance on key label elements and *PLL* submission and review process.

Look-Alike, Sound-Alike Drug Product Names

Where a brand name is proposed, a look-alike, sound-alike (LA/SA) assessment is required as part of the submission information to evaluate product label safety and effectiveness. This assessment of orthographic similarities when written or similar phonetics when spoken is to determine whether health product names are likely to be confused with one another, potentially causing prescribing, transcription, dispensing, administration and/or self-selection errors.

The pre-authorization authorities for this are in *FDR* Sections C.01.014 and C.08.002 for old and new drugs, respectively. If confusion between the proposed brand name and other brand, common or proper names is deemed likely, Health Canada may refuse to issue a marketing authorization. For drugs already on the market, Health Canada may suspend an NOC under C.08.006(2)(f) if the manufacturer has

not corrected a brand name problem following written notice, or direct the manufacturer to stop sale under C.01.013 if supporting safety evidence is not provided within a defined timeline.

Currently, this requirement applies to prescription pharmaceuticals, Schedule D products (biologics), Schedule C products (radiopharmaceuticals, kits), drugs sold directly to healthcare professionals and intended for professional use and drugs sold to the general public with healthcare professional intervention. It may be required for nonprescription products if the proposed brand name is not exclusively descriptive per the proposed claim(s) and/or proper or common name(s) of the ingredient(s) in the product.

Guidance Document for Industry: Review of Drug Brand Names applies to prescription pharmaceuticals, Schedule D products (biologics), Schedule C products (radiopharmaceuticals, kits), drugs sold directly to healthcare professionals and intended for professional use and drugs sold to the general public with healthcare professional intervention. The guidance clarifies when LA/SA assessments are required, Health Canada's timing and overall assessment process within the drug submission review. Expectations surrounding the analysis search, simulation and synthesis are addressed within Canadian context.

Further information is provided in *Frequently Asked Questions—Guidance Document for Industry: Review of Drug Brand Names*.

Contact Information Requirement

Contact information is required to ensure Canadians have label information allowing them to contact someone responsible for the product in Canada if they experience a problem or have a question or concern. The contact needs to be in Canada. A toll-free number, email address or website is the recommended contact method.

Contact information should be on inner and outer labels to ensure access even if the outer packaging has been discarded. Exemptions for small containers and special containers apply.

This requirement applies to prescription and nonprescription pharmaceutical drugs and those administered or obtained through a health professional. It does not apply to biologic drugs or radiopharmaceuticals.

Mock-Ups

Mock-up requirements are addressed in *FDR* C.01.014.1(2)(m.1), C.08.002(2)(j.1), C.08.003 (3.1)(a)(ii) and C.08.003 (3.1)(b)(ii). The requirement to submit this information allows Health Canada to review label design elements in addition to regulatory requirements.

Where there is a deviation from expectations outlined in Health Canada guidance, a written rationale should be provided in a note to the reviewer.

When drug submission review targets are ≥ 150 days, the initial *PLL* review usually occurs in the first 90 days. If review timelines are shorter, design elements and regulatory requirements are reviewed at the same time. A final review occurs prior to NOC or DIN issuance to address any content changes resulting from the review. The final mock-ups submitted during review are considered the final version for approval. As a result of these process changes, final labels no longer need to be submitted after the drug is available for sale.

Depending on the product type, the following documents are submitted:

- Labels and Packages Certification Form for Prescription Drugs
- Labels and Packages Certification Form for Nonprescription Drugs
 - Certification forms are included at filing and certify such items as the translation fidelity, commitment to provide a second language product monograph or prescribing information and/or second language package insert within the first 20 days of acceptance into review, commitment to update the same during review and to file the final version no later than 20 days after the NOC, No Objection Letter (NOL) or DIN is issued, certification as to font size and type style of mock-up labels and package insert and to content of first and second language package inserts.
 - inner and outer label mock-ups
 - package insert mock-ups
 - product monograph or prescribing information (not in mock-up format)

Note that mock-ups should be provided with proposed text and design elements as actual size, color, editable pdfs with dimensions noted. Placeholders for the DIN, lot number and expiry date should be created, as applicable, using an approved format. If the package has a novel label format, a photograph (or alternative visual representation) of the package should be provided, with all sides visible, including vial, cap and ferrule, as applicable. Further details on mock-up requirements and timing in different situations are addressed in the Q&A guidance documents for both prescription and nonprescription drugs.

A more detailed discussion of *PLL* requirements for nonprescription drugs is presented in Chapter 9.

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Recommended Reading

- *Food and Drugs Act*. Justice Laws website. <https://laws-lois.justice.gc.ca/eng/acts/F-27/index.html>. Accessed 1 October 2019.
- *Food and Drug Regulations*. Justice Laws website. https://laws-lois.justice.gc.ca/eng/regulations/C.R.C.,_c._870/index.html. Accessed 1 October 2019.
- *Good Label and Package Practices Guide for Prescription Drugs* (June 2019). Health Canada website. <https://www.canada.ca/en/health-canada/services/drugs-health-products/reports-publications/medeffect-canada/good-label-package-practices-guide-prescription-drugs-profile/guidance-document.html>. Accessed 1 October 2019.
- *Guidance Document Questions and Answers: Plain Language Labelling Regulations for Prescription Drugs*. Health Canada website. <https://www.canada.ca/content/dam/hc-sc/documents/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/questions-answers-plain-language-labelling-regulations/questions-answers-plain-language-labelling.pdf>. Accessed 1 October 2019.
- *Good Label and Package Practices Guide for Non-prescription Drugs and Natural Health Products* (June 2018). Health Canada website. <https://www.canada.ca/en/health-canada/services/drugs-health-products/reports-publications/medeffect-canada/good-label-package-practices-guide-non-prescription-drugs-natural-health-products.html>. Accessed 1 October 2019.
- *Frequently Asked Questions—Guidance Document for Industry: Review of Drug Brand Names*. Health Canada website. <https://www.canada.ca/en/health-canada/services/drugs-health-products/reports-publications/medeffect-canada/frequently-asked-questions-guidance-document-industry-review-drug-brand-names.html>. Accessed 1 October 2019.
- Ibid.
- *Guidance Document: Labelling of Pharmaceutical Drugs for Human Use* (13 June 2015). Health Canada website. <https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/labelling-pharmaceutical-drugs-human-use-2014-guidance-document.html>. Accessed 1 October 2019.
- *Regulations Amending the Food and Drug Regulations (Labelling, Packaging and Brand Names of Drugs for Human Use)*. Canada Gazette website. <http://www.canadagazette.gc.ca/rp-pr/p2/2014/2014-07-02/html/sor-dors158-eng.html>
- *Guidance Document: Questions and Answers: Plain Language Labelling Regulations for Non-prescription Drugs* (September 2018). Health Canada website. <https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/guidance-document-questions-answers-plain-language-labelling-regulations-non-prescription-drugs-contact-lens-disinfectants.html>. Accessed 1 October 2019.