Good Label and Package Practices Guide for Prescription Drugs

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Canada

Health Canada is the federal department responsible for helping the people of Canada maintain and improve their health. We assess the safety of drugs and many consumer products, help improve the safety of food, and provide information to Canadians to help them make healthy decisions. We provide health services to First Nations people and to Inuit communities. We work with the provinces to ensure our health care system serves the needs of Canadians.

Preamble

The utmost care has been taken to ensure the accuracy of information presented in this guide. The guide reflects the information available during its development and is meant to provide initial considerations when preparing the content and design of labels and packages. It is anticipated that new research on various topics addressed in this guide will become available in the future, and revisions may be warranted to integrate such new information.

This document should be read in conjunction with the relevant sections of other applicable Health Canada regulations, guidance documents, and policies.

Organization of the Guide

The guide is divided into three parts:

> *Part 1* presents the objective, introduction, and scope. It also provides an overview of the process used in developing the guide.
>
> *Part 2* highlights the importance of the user's perspective. It emphasizes the need to consider the environment in which health products are selected and used. This is intended to provide a reference point for all other sections of the guide.
>
> *Part 3* addresses the specific components applicable to the design of labels and packages from a safety perspective. The section for each component presents background information followed by recommendations.

The appendices contain supplementary information to the guide as follows:

> Appendix 1: Glossary
> Appendix 2: Human Factors Principles and Assessment Methods Relevant to Labelling and Packaging
> Appendix 3: Product-Use Process Maps
> Appendix 4: Acknowledgements

All parts of the guide and its sections should be considered together, i.e., no topic is to be considered in isolation.

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1 Overview of the Guide

1.1 Objective

The objective of the Good Label and Package Practices Guide for Prescription Drugs is to provide direction to sponsors, manufacturers and license holders (to be referred to as 'sponsors' within this guide) in designing safe and clear labels and packages.

It is essential that all labelling and packaging regulatory requirements be met.

The recommendations provided in this guide will aid sponsors in the organization of (a) information required by the regulations, and (b) other complementary information important to the proper identification, selection, and use of the product. The information is presented to support the design and development of labels and packages that are clear, effective, and minimize the risk of errors causing harm.

1.2 Introduction

The label and package are the first points of interaction between a health product and a healthcare professional or patient. They communicate key information about the safe and proper use of health products, and are important aids in product identification, selection and administration. The ability to perform product identification, selection and administration safely is dependent on the user being able to read and understand the information on the label.

Through the Plain Language Labelling Initiative, new *Regulations Amending the Food and Drug Regulations (Labelling, Packaging and Brand Names of Drugs for Human Use)*[1] have been introduced with the intention of improving the safe use of drugs by making drug labels easier to read and understand. These amendments include a requirement for the addition of contact information on the label and the submission of label and package mock-ups. The content presented in this guide will provide information that supports the objectives of the Plain Language Labelling Initiative.

1.3 Scope

This guide focuses on the inner and outer labels and packages across the following health products for human use:

- prescription pharmaceuticals;
- biologics and radiopharmaceuticals; and
- drugs that are permitted to be sold without a prescription but that are obtained or administered only under the direction of a healthcare professional (e.g., exempted codeine preparations per the *Narcotic Control Regulations* 36(1)[181], nitroglycerin, insulin, injectable epinephrine for anti-allergic purposes).

Any of these may be referred to as a "product" or "health product" in the context of this guide.

This guide is not applicable to whole blood and its components under the *Blood Regulations*[2]; cells, tissues and organs under the *Safety of Human Cells, Tissues and Organs for Transplantation Regulations*[3]; consumer health

products for self-selection; disinfectant drugs; drug products used in clinical trials; active pharmaceutical ingredients; and drug products for veterinary use.

The guide complements Health Canada's Guidance Document: Labelling of Pharmaceutical Drugs for Human Use[4] and complies with the *Food and Drugs Act*, *Food and Drug Regulations*[5].

Aspects of product labelling that are not covered include the naming of health products (refer to Guidance Document for Industry – Review of Drug Brand Names[6]), user-applied labels, product monographs, package inserts (e.g., prescribing information), and Patient Medication Information.

1.4 Content contributing to guide development

A large volume of information has been published providing direction to optimize the design and content of health product labels and packages to support safe use. This body of knowledge, along with additional research and consultation on the topic, has been reviewed and adapted to produce this guide and is inclusive of the following:

- Applicable Canadian regulations, standards, policies, and guidelines
- Health Canada risk communications applicable to inner and outer labels and packages
- Package and label changes and relevant learning from published reports of safety incidents with labels and packages identified as a contributing factor
- Aggregate analysis of error reports voluntarily submitted to the Institute for Safe Medication Practices Canada in which sponsor's labels or packages were explicitly identified as a concern or a contributing factor[7,8]
- Consideration of human factors issues and principles (refer to Appendix 2, "Human Factors Principles and Assessment Methods Relevant to Labelling and Packaging")
- Applicable international regulations, standards, policies, and guidelines
- Concepts applied to labelling and packaging of health products by safety organizations (e.g., the United Kingdom's National Patient Safety Agency - now part of the National Health Service)
- Engagement of an international, multidisciplinary expert advisory panel and other relevant stakeholders and experts (refer to Appendix 4, "Acknowledgements")

2 Considering Users and Their Environments

The design of a health product should meet the user's needs within the environment of use, rather than there being an expectation that the user or the environment of use will change to fit the intended use of the health product.[9] Design the glove to fit the hand, instead of expecting the hand to fit a particular glove.

The environment of use can influence how users interact with a health product, so consideration of the environment should be incorporated into the design and evaluation of health product labels and packages.[9] From a prescription drug perspective, the environment of use can include where the product will be used (e.g., hospitals, long-term care facilities, healthcare professionals' offices, emergency transport settings), where the product will be stored, types of supporting tools and technologies (e.g., dose organizers and dispensers, medication administration records, bar-coding technology), and lighting level.

It is important that product labels and packages be designed with the user in mind and with consideration of the environment and processes in which the product will be used (stocked, selected, and administered). A recent aggregate analysis of labelling and packaging incidents involving health products offered an overview of some of the issues that users of health products have experienced.[8] The following are some of the potential contributing factors identified in that analysis:

- look-alike labelling and packaging
- prominence of trade dress and brand name
- lack of prominence of proper or common (non-proprietary) name
- lack of prominence (and lack of clarity) of expression of strength
- legibility and readability of information (e.g., type size, contrast of print against background)
- confusing layout of label
- lack of coordination between display of information and perforations on blister packs
- use of dangerous or misleading abbreviations

3 Designing Labels and Packages for Safety

3.1 Introduction

Part 3 of this guide presents information on current good practices in the design and layout of a health product label, the information contained on the label, and the design or choice of package. The topics and principles cover various contributing factors in reported medication incidents and issues identified by environmental scans of sponsors and users.

Although the various topics are presented separately within Part 3, they must be considered together to achieve a balance between standardization and differentiation (e.g., within a sponsor's product line). Standardization of product labels and choice of packages can reduce errors by reinforcing the pattern recognition on which humans rely when processing information.[10] However, the more label or package characteristics that products have in common (e.g., type style, size and colour of type, size and shape of container or package, layout of information), the more likely that products will look alike. The cumulative effect of individual label and package characteristics can result in look-alike issues that make it difficult for users to distinguish one product from another. The potential for look-alike issues should be considered during the design phase of a product's labelling and packaging. Similarly, changes to existing product labels and packages should strike a balance to prevent introduction of new look-alike issues. Achieving a balance between standardization and differentiation is particularly important to prevent (or resolve) look-alike issues that involve high-alert medications or a sponsor's higher-risk products.

In addition to all the topics discussed in the guide, sponsors are strongly encouraged to consider human factors aspects of product selection, use, and handling, as well as user testing with a risk based approach (refer to Appendix 2, "Human Factors Principles and Assessment Methods Relevant to Labelling and Packaging"), in the design of labels and packages.

3.2 Planning the design of labels and packages

When designing product labels and packages, sponsors are strongly encouraged to undertake a number of steps. The following is an overview of the steps that sponsors can incorporate into existing product development and marketing processes:

- Consider the design of health product labelling and packaging as early as possible in the development process.
    - Development of the package should begin early. Factors influencing the choice of a package should go beyond maintenance of stability, ease of manufacturing, or marketing considerations. The package design will also affect the size of both inner and outer labels.
    - For products gaining approval in Canada, the sponsor may already have experience in other markets. Carefully review complaint and incident data to determine if changes are needed for the planned label or package of the health product for the Canadian market.
- Identify the users of the product and their environments of use.
    - Designing a label and package for safe use requires keeping the users and the environments of use at top of mind throughout product development.

- At a minimum, review the questions in Appendix 2, "Human Factors Principles and Assessment Methods Relevant to Labelling and Packaging", to identify the users and environments of use. These questions are intended to elicit a wide range of considerations, and their answers can provide opportunities to understand factors important to safe design.
- Product-use process maps can be helpful when human factors-based user testing is planned, in that such maps will help in identifying the scope of use and the primary users. (Refer to Appendix 3, "Product-Use Process Maps" for an example.)
- Consider other products that might be used simultaneously with the product of interest, as products are rarely used in isolation.

- Consider user testing. A variety of user testing and other methods have been applied to the design and redesign of labels. (Refer to Appendix 2, "Human Factors Principles and Assessment Methods Relevant to Labelling and Packaging".)
- Prepare mock-ups of the label and package, including the outer packaging. Mock-ups can have multiple uses (e.g., user testing, focus groups).
- Use a continuous improvement approach. Review complaint and incident data to identify challenges and unanticipated label or package problems early in the design process and following marketing. Manufacturers should monitor trends and implement risk-mitigation measures to improve labels and packages. Gathering information throughout the product life-cycle is a proactive approach and can assist with package and label design.

3.3 Design and layout

3.3.1 Type style and size

Background

Illegibility of printed information is a contributing factor in health product errors.[8,11] Interactions between or changes to typographic elements on a label (e.g., type style, size, spacing, use of bold or italic, colour, contrast) can affect both legibility and comprehension.[12] Label information must be legible to users in the real-world environments or situations in which products will be used.

Recommendations

The following recommendations do not apply to trademarks, copyrighted text, and logos.

Type Style (Typeface)
- When choosing a type style, consider that different styles of the same point size do not appear the same in size.[12]

Calibri	9 point
Arial	9 point
Arial Black	**9 point**
Univers	9 point
Verdana	9 point

- Use of a sans serif type style (e.g., Univers, Helvetica), that is not compressed, expanded, or decorative is preferred for key information.[13] A sans serif type style has no decorative extensions, is crisper and

cleaner, and typically appears larger than a serif style of the same point size.[14] Compressed or condensed fonts may be more difficult to read, even with a larger point size.[12]

- Choose a type style with adequate spacing between letters (to enhance legibility) and between words (to enhance readability).[12] Narrow letter and word spacing can cause apparent merging of words, whereas extremely wide spacing can be disruptive to the reader.[12] Adequate spacing can also reduce possible illegibility if ink were to bleed.
- Avoid using all capital letters[12,13,15,16] (exceptions: brand names, headings, and warnings that are brief may be fully capitalized). (Refer to section 3.4.3, "Critical Warnings".) The use of all capital letters reduces legibility and adversely affects readability to a greater extent than any other factor. Lowercase characters have more variation (e.g., letter shapes) in their features, which results in better legibility.[12]
- Avoid the use of italic type except to emphasize a particular portion of text.[12]

Type Size

- Use a type size that can be read easily by a variety of users (e.g., elderly people, those with visual impairment) in environments where products will be used (e.g., in a hospital room with low lighting). The following examples show one type style in various point sizes to illustrate that small changes in point size can affect readability:

  this is Verdana 4.5 point
  this is Verdana 6 point
  this is Verdana 8 point
  this is Verdana 9 point
  this is Verdana 10 point
  this is Verdana 12 point

- The largest type size possible is recommended. However, a point size less than 6 should not be used for key information.[13,17] Key information includes the key elements (refer to section 3.4.1, "Key Elements on the Principal Display Panel") and label information required by regulations.
    - For very small prescription products, such as ampoules and vials of 2 mL or less, the type should be at least 1.5 mm high.[15]
- To enhance legibility when using smaller type sizes (e.g., on small containers), consider using a background colour that is significantly different from the type colour.[17] (Refer to section 3.3.5, "Colour and Contrast" for further information.)
    - Type of very small size may be made more easily readable in combination with other characteristics, e.g., font, colour, white space, bolding, etc.
- The *Food and Drug Regulations* require that the type of the proper or common name be, at a minimum, half the size used for the brand name.[18]

General Formatting

- To enhance readability, use flush left, ragged right alignment of multiple lines of text (as in this document). This form of alignment provides visual points of reference that guide the reader's eye smoothly from line to line. Since each line is either shorter or longer than the next, the eye is cued from one to the next.[12]
- To enhance the readability of information, use bullet lists, with items in point form instead of complete sentences, if possible.[13]
- When providing stepwise directions, use numbered lists and keep all text for each individual step on one line, if possible. This makes it easier for users to follow the instructions and enables them to find their place again if interrupted.[13]

- Use contrasting characteristics (e.g., type size, weight, bolding, colour, and spacing) to help users distinguish one product from another, and to highlight important information (e.g., warnings in the directions for use) to facilitate safe use of the product, and enable the user to quickly find the information needed.[13] For example, if it is necessary to present information in paragraph form, use of bold type for key words or phrases or use of subheadings can make it easier and quicker for users to find the information they need.[13] The following example shows how bold type or subheadings might be used on a product label:

  Usual Adult Dose: 75 mg (1 tablet) once daily.

  Product monograph available upon request. **Store tablets between 15° and 30° C**. Protect from moisture.

  Pharmacist: Dispense with enclosed Patient Information leaflet.

- Consider the information provided in the Canadian Standards Association (CSA) standard Labelling of Drug Ampoules, Vials and Prefilled Syringes,[15] which may be helpful for selecting aspects such as type style (including character width and height), stroke ratios, and spacing between characters, words, and lines.

3.3.2 TALLman lettering

Background

TALLman lettering is a method used to assist in the differentiation of look-alike, sound-alike non-proprietary (proper or common) drug names through the application of UPPER CASE lettering to certain syllables or groups of letters within names.[9,19] TALLman lettering has typically been applied to drug names to bring attention to the points of dissimilarity between confusable names.[19] TALLman lettering may be effective because it draws attention to drug names presented in this format and can act as a warning.[20] Overuse of the technique may reduce its effectiveness as names may no longer appear novel.[21]

TALLman lettering is only one of many risk mitigation strategies that can be implemented to minimize errors between confusable product names. This technique does not rely on type style, point size, or colour and can be accommodated in electronic systems; for these reasons, it has become a widely accepted method of distinguishing among drug names within healthcare practice settings.[22]

The Institute for Safe Medication Practices Canada (ISMP Canada),[23] the Institute for Safe Medication Practices (US),[24] the US Food and Drug Administration (FDA),[9,24] and various other organizations around the world have supported the application of TALLman lettering for potentially confusable drug names.[22,25-30]

Recommendations

- Use TALLman lettering on product labels only if it is intended as a risk mitigation strategy for an identified safety concern, i.e., if there is an identified risk of confusion between **two or more** drug names with potential for serious consequences.
- Use TALLman lettering as a safety strategy, not a marketing strategy.
- To ensure that the effectiveness of TALLman lettering is not diluted and that it has the greatest possible impact, limit its use to those names associated with the potential for high risk to patient safety. These names should be identified through a risk assessment process.[20],[29]

- The potential root causes for drug name confusion should be understood before TALLman lettering is considered as a potential solution. If the confusion arises from look-alike labelling or packaging, alternative differentiation strategies should be applied.
- Ensure that TALLman lettering is consistent with the ISMP Canada list of TALLman Lettering for Look-Alike/Sound-Alike Drug Names in Canada.[23]
- If used, TALLman lettering should be applied only within the **non-proprietary name** or within the **non-proprietary portion** of the brand name on product labels.
- Whenever TALLman lettering is used, apply it to both the inner and outer labels, for consistency.

3.3.3 Proximity and compatibility of information on the principal display panel

Background

The Proximity Compatibility Principle specifies that all information relevant to a common task or mental operation should be displayed close together.[31,32] For example, the name, strength and dosage form are distinct but closely related elements used to identify and administer a health product and would be placed in close proximity on a product label. Conversely, the net quantity in the package is not related to this information or needed to identify and administer the product and would therefore be placed in a separate location. Confusion errors have been reported when the product strength (a numeric value) and the unit or pack size (another numeric value) were placed in close proximity.

Proximity and compatibility can be affected by other label and type attributes, such as colour, type style, and type size and weight. Use of the same colour(s), type style, point size, and markings or graphics can inadvertently link pieces of information (e.g., numeric values) even when there is physical distance between them on the label.

Recommendations

- Place items that are relevant to a common task or mental operation (e.g., health product name, strength, dosage form, route of administration) close to one another on a product label.[32,33]
- Consider how the various elements of the label are presented as a whole. In addition to grouping closely related information together on the principal display panel, consider how the colour, type style, and type size and weight visually separate or connect different pieces of information. For example, if the number of tablets in a package (unit pack size) is presented in the same colour as the product strength, but has a more prominent appearance (e.g., in bold type or larger type size); the number of tablets may be misinterpreted as the strength or dose.
- When listing more than one strength on a single panel, ensure that the strength per unit is placed in close proximity to the strength per total volume.[16,33] When the total quantity per total volume is present on the principal display panel, ensure that this information is more prominent than any other expression of strength.[26,78]
- List the net quantity in the package separately from, and less prominently than, the product strength. Displaying this information together (e.g., 10 mg / 7 tablets) has been a contributing factor in medication errors.[8] The number of units can remain on the principal display panel but should be separated either physically or through design features so to reduce the chance for it to be misread as the product strength.

- Avoid separating unrelated information with marks that could be misinterpreted. For example, if a point or a dash is positioned between the dose and the total volume in the container, the volume might be misinterpreted as part of the dose (e.g., "1000 units ● 25 mL", where "25 mL" refers to the total volume in the container, not the strength per total volume, and might be interpreted as "1000 units **per** 25 mL").
- When possible, avoid placing unrelated information (including graphics) between the product name and its strength.[9,26]
- To ensure that key information is legible and not subject to misinterpretation, avoid superimposing text and images (or logos).[35]
- List the standard of manufacture, as applicable (e.g., United States Pharmacopeia [USP], British Pharmacopoeia [BP]), in close proximity to a product's proper name.[4]

3.3.4 White space

Background

White space is an important aspect of design and requires careful consideration during the design phase. It should be used as liberally as possible to enhance the readability of health product labels,[140] so that healthcare professionals and patients can quickly find the information they need to facilitate safe product use.[13]

The term "white space" does not necessarily refer to space on a label that appears white. Depending on the background colour, it may be more accurate to use another term, such as "blank space". Such white space on a health product label or package refers to any space not covered by print, markings, coloured graphics, watermarks, or other elements of the label.

White space surrounding text can create a feeling of openness.[36] It can also help readers to focus on what they are reading.[14] Importantly, it may improve readers' willingness to read and their ability to find and process the information presented, because it helps to reduce the concentration and mental workload required.[36,37]

Recommendations

- Incorporate white space as part of the design and layout of information on health product labels as early as possible in the design process. White space should be used for the following purposes:
  - to frame a particular grouping of text (e.g., bulleted lists) and to separate unrelated information
  - to separate one sentence from another
  - to separate paragraphs (to help distinguish one idea from another)
  - around headings and key information (e.g., warnings) to emphasize their importance
- Maximize the use of white space to avoid crowding information on the label when smaller type size is used. Increasing the space between lines may be especially helpful for elderly users.[14]
- Avoid using a condensed type style, which reduces white space between letters and words and which can reduce legibility by causing words to merge together visually.[12]
- For the labelling of drug ampoules, vials, and prefilled syringes, particularly for spacing between characters, words, and lines, refer to the CSA standard, Labelling of Drug Ampoules, Vials, and Prefilled Syringes.[15]

3.3.5 Colour and contrast

Background

Colour on the inner and outer labels of health products must be carefully applied to help, and not hinder, the selection of appropriate products by users. The application of colour is just one of many factors to be taken into account in the design of health product labels and should not be considered in isolation.

People with normal colour vision are able to detect differences between similar colours only when the colours are placed side by side. Without side-by-side comparison, similar colours cannot be easily distinguished, and errors can be made if colour is the only variable used on a health product label. For example, problems may arise if different strengths of the same product are differentiated by using variations of one specific colour.[12]

In addition, under less-than-optimal conditions, the ability to discern colours can be further reduced, for example, when print appears on small containers or labels, when viewing time is short (e.g., urgent situations, distractions), when a lower level of lighting is used (e.g., in a patient's hospital room at night[38]), and when colours of similar products are physically separated (i.e., not viewed together).[39]

The effect of colour in label design can be affected by colour-blindness.[5,25,38,43-45] Certain types of colour-blindness are more common than others. Colour-blind users may have limitations in their perception of specific colours[35,38] (e.g., red-green) or may have difficulty in reading text in particular colour combinations or on particular colour backgrounds[39].

Contrast
Contrast is a fundamental design principle that is used to help the user detect differences in what is seen.[44] It is an important factor for the readability of text, particularly on packages with a coloured background.[1,9,10,16,33,35,41-48] For example, it has been recommended that text of a dark colour be used on pale backgrounds to ensure sufficient contrast for optimum visibility.[9,10,15,16,35,47,49]

Colour Differentiation and Colour-Coding
Colour differentiation is generally used to highlight particular features on a product label or to help distinguish one product from another.[10,78] However, repeated use of this particular technique can lead to look-alike product labels,[10,35,45,49] which can in turn predispose users to confirmation bias (i.e., users see what they expect to see). Colour differentiation can also reduce the prominence of key information if it is not used skilfully.[15,45]

"*Color coding* is the systematic application of color to aid in classification and identification. A color-coding system enables users to associate a color with a function."[10] Colour-coding relates to the use of consistent colours for specific products or product strengths **by all manufacturers.** For various reasons, many safety experts do not support the use of colour-coding:[9,10,16,35,41,50,51]

- the lack of supporting evidence that it is an effective means to prevent errors,[16,50]
- the known problems that have resulted from colour-coding,[9,10,50,51]
- the inherent limitations of selecting identifiable colours,[35,38,39,50-52] and
- the limitations of human memory.[10,39,50]

Colour-coding appears to have some benefits for user-applied labels and in specific practice areas, such as by anesthesiologists in the operating room setting,[53] but these benefits are not necessarily applicable to other users or other environments. Users should not be expected to remember and attribute meaning to particular colours, especially given the large number of different product strengths and concentrations, the thousands of drug classes and products, and the limited number of visually distinct colours.

By convention, some colours are typically recognized as conveying certain meanings (e.g., red may convey danger, orange may convey a warning, yellow may convey the need for caution).[39] Such conventions are commonly used for signage in dangerous or hazard-prone environments, e.g., for traffic signs or for containers holding hazardous chemicals.[54] Aside from these examples, subjective meanings for colour may also exist in specific populations of users.[55]

Recommendations

Use of Colour
- The application of colour is just one of many factors to be taken into account in the design of health product labels and should not be considered in isolation.
- Consider the users' environments, because a given colour may appear different under different lighting conditions.[9,35,38,41,42]
- Colour choices should take into account the following general principles:
  - *Hue:* Colours opposite each other on the colour wheel (e.g., blue and orange, yellow and violet) are considered to have more contrast than colours closer together on the wheel (e.g., violet and blue, orange and red) and therefore provide greater differentiation in hue.[52,56-58]
  - *Saturation:* Fully saturated (bright) colours combined with low-saturation (dull) colours provide greater contrast than combinations of colours of a similar saturation level.[56]
  - *Value:* Colours with a low value (dark colours) placed beside or against colours of a high value (light colours) have greater contrast than colours with similar values.[52]
- Use colour for the following purposes:
  - to draw attention to important label information,[10] such as the name of a health product and its strength[33]
  - to bring attention to or enhance the prominence of warning statements[9,10,58]
  - to differentiate one product from another[41] or to differentiate between strengths within a product line[41,45,50,59]
- While trade dress and logos can assist in the selection process, care must be taken to appropriately differentiate products within a product line to decrease the potential for confusion.
- To enhance differentiation among product strengths, use a colour with a different hue, rather than a different intensity or value of the same colour.[16] For example, avoid using different shades of blue for various strengths, and instead use distinctly different colours.
- As a general principle, colour-coding of health products is not recommended.[9,10,16,35,41,50,51]
- Consider using more than just colour to distinguish between products.[9] Other techniques for differentiation include colour bands, frames or key lines (i.e., boxes around text).[37]
- When selecting colours for labelling and packaging, consider the potential implications of colour-blindness (e.g., avoid using both red and green together,[5] because they may not be easily distinguished by those with red-green colour-blindness). Computer simulation programs, such as Vischeck,[60] may be

used to determine how colours will be perceived by individuals with different forms of colour-blindness.

- Match the styles of inner and outer package labels so that the visual appearance, including use of colour, is identical or related.[35,45] This approach can help to ensure that users (re)place an inner container into the correct outer package as needed. It can also help users to identify the corresponding outer (secondary) packaging when they need information that may be available only on that outer package (e.g., directions related to a health product in a small-volume container). Such matching between a container label and its outer package or box label reduces the amount of information that needs to be processed simultaneously by the user.[61]

Contrast
- Maximize the legibility of text by ensuring good contrast between text and background [9,10,33,42,45,62] (e.g., apply dark text on a pale background[16,41,47,48]). Avoid the use of type and background colour combinations that are known to be very difficult to read (e.g., black or yellow type on a red background[47]).
- Use opaque labels on clear or translucent containers to ensure that type is legible and does not show through the container.[35] Ensure that sufficient clear area remains after application of the label to allow the user to view the contents of the container.[35]
- If a paper label is not an option, use contrasting type ink on an opaque background on the translucent container to maintain readability.[35]
- Engraving (i.e., embossing and debossing) of type onto a container may not provide sufficient contrast on its own; therefore, if such methods are used, highlight the type with ink.[16]
- Ensure that any symbols required by regulations have sufficient contrast against the background colour.[18]

Containers
- Graduation scales on prefilled syringes (i.e., "ready-to-use" clear containers) or oral dosing devices (e.g., oral syringes) should be easily legible. For example, use black ink on a white field of view.[15]
- For blister packs, use a non-reflective material for the backing, so that information is legible.[9,26,45]
- For liquids in clear containers, affix labels with colourless glues to prevent misperception of container contents as being discoloured.[15]

3.3.6 Use of abbreviations, symbols, and dose designations

Background

The use of certain abbreviations (e.g., OD), symbols (e.g., µ), and dose designations (e.g., 1.0 mg) to convey health product-related information has been identified as an underlying cause of serious, even fatal errors.[63] An abbreviation may have more than one meaning and may therefore be susceptible to misinterpretation,[9] particularly if users are unfamiliar with the intended meaning. Practices and terminology may vary among different healthcare professionals and groups (e.g., pharmacists, nurses, physicians), as well as between clinical specialties, or even between patients and healthcare professionals.

Recommendations

General

- Minimize use of abbreviations, symbols, and dose designations in health product packaging and labelling.[9,63]
- Avoid the use of **error-prone** abbreviations, symbols, and dose designations.[9,63] Refer to ISMP Canada's "Do Not Use" list[63] for further details. This list (adapted from a list prepared by ISMP US[64]) takes into account medication errors voluntarily reported to ISMP Canada for which the reporter identified an abbreviation, symbol, or dose designation as a potential contributing factor in incidents causing harm or having the potential to cause harm.
- Ensure that any abbreviations used provide information that is useful and easily identifiable to the users (i.e., healthcare professionals, patients).[6]
- An abbreviation should not be ambiguous or otherwise have the potential to be misinterpreted by the user. In particular, avoid abbreviations that indicate dosing schedules. (For example, "QD" may be read or misinterpreted as "QID", and "OD" may be interpreted as either "oculus dexter" [Latin, meaning "right eye"] or "once daily").[6]
- Use international or national standards for abbreviations (e.g., abbreviate "milliliters" as "mL"[63]). **Note:** The symbol "μg" (meaning "microgram") conforms to the International System of Units (SI) and is often used in scientific literature. However, for labelling purposes, the abbreviation "mcg" should be used instead.[4] The Greek letter "μ" may be difficult to see in some print and size formats and may be misread as the letter "m" (i.e., "mg" for "milligrams", rather than the intended "μg" for "micrograms").
- The proper or common names of health products and any medicinal ingredients in the product should not be abbreviated.[4,15,16,62] Product confusion errors can result when similar abbreviations are used for multiple products (e.g., MSO_4 [morphine sulfate] and $MgSO_4$ [magnesium sulfate]).
- Whenever possible, avoid the use of abbreviations on vaccines (e.g., Tdap and DTap). Abbreviations have been identified as contributing factors in vaccine selection errors.[66]
- Define abbreviations used on any product dose delivery devices provided. Ensure that abbreviations used on such devices are consistent with abbreviations used on product labels and packaging, such as label directions, outside packaging (carton labelling), containers, and any accompanying written materials.
- Comprehension testing for any new abbreviation is highly recommended. (Refer to Appendix 2, "Human Factors Principles and Assessment Methods Relevant to Labelling and Packaging".)

Route of Administration

Express in full any uncommon route of administration (e.g., intrathecal), as it may be unfamiliar to users and use of an abbreviation may result in confusion.[26] Other abbreviated routes of administration should be explained in full at least once if used elsewhere in the labelling.[4]

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3.3.7 Bilingual labelling

Background

Bilingual labelling may pose challenges for the readability of inner and outer labels because of the possibility of crowding of information. Healthcare professional, patient, and consumer feedback gathered in the development of the guide highlighted the following concerns:

- ensuring adequate space for both English and French text, while preserving white space especially when space is restricted (e.g., small containers). French text tends to be slightly longer than the corresponding English
- ensuring accuracy and meaning of health product information is preserved in both languages
- ensuring standardization and consistency of formatting for bilingual text on health product labels (e.g., product name, salt forms of the drug, placement of certain pieces of information, prominence of specific information)
- recognizing subtle differences between English and French in how information is presented and interpreted (e.g., use of a period [English] or a comma [French] to denote the decimal)

Recommendations

General Principles
- Consider bilingual labelling early in the label and package development process, to accurately determine the amount of label space needed to accommodate required product information.
- Inclusion of both languages on the label (and within a technology, e.g., automated voice instructions) is preferred.
- If including English and French on the same panel where space is limited, consider how best to display key information in a consistent manner, within and across product lines. (Refer to Appendix 1, "Glossary" for definition of key information.)

Organization of Information
- For product packages or containers with multiple panels or sides (e.g., an outer box), it is preferable to dedicate an entire label panel for information in English and another for information in French.
- Where packages have only one or two panels available or packages have limited space, consider using different types of labels or innovative labels (e.g., peel-back labels) to accommodate information in both languages. Novel label formats should comply with applicable regulations and guidance documents.[1,4] (Refer to section 3.5.2, "Small Containers and Small-Volume Containers".)
- Identify commonalities in English and French for the key information, and determine if the information can be combined to save space. When information (i.e., the drug name) is the same in English and French, consider combining this, instead of repeating all details in both languages.

Expression of Strength or Concentration
- For large numbers (greater than 9999), use a thin space, rather than a comma, to separate digits into groups of three (e.g., 10 000). (Refer to section 3.4.2, "Expression of Strength".)

- Although in English a comma is frequently used to separate groups of digits in large numbers (e.g., 10,000), in French a comma may be used to denote the decimal point. The meaning of a comma may therefore be unclear for some users.[65]
- According to the SI system of units, a decimal or decimal marker "shall be either the point on the line or the comma on the line" and "for numbers with many digits, the digits may be divided into groups of three by a thin space, in order to facilitate reading. Neither dots nor commas are inserted in the spaces between groups of three."[65]
- Ensure that the gap between numbers is large enough to indicate that the numbers are grouped in threes, but not too large, so that the groupings will still be interpreted as representing one number.

- Consider how to standardize the display of product concentration when the unit of measure differs in the two languages (e.g., "units" in English, "unités" in French). Considering the commonalities of key information may help for combining information.
- For product packages with no distinct panels or sides (e.g., ampoules, vials), take into account the field of view available for the key information. (Refer to section 3.4.2, "Expressions of Strength", for more than one expression of strength on a label.)
- The CSA standard, Labelling of Drug Ampoules, Vials and Prefilled Syringes, also provides direction on how French and English may be applied to ampoules, vials, and prefilled syringes.[15]

3.3.8 Logo, branding, and trade dress

Background

- Whereas logos, trade dress and branding can assist in differentiating products from different manufacturers, incident reports have indicated that they have the potential to contribute to errors and impede the safe use of health products.[8] The following issues, among others, have been identified:
- Trade dress may be a factor in look-alike labelling and packaging, particularly for
  - products from the same sponsor
  - items across a product line[8]
  - generic products, where there appears to be a tendency to create or standardize a look across all product lines[8,67-69]
- A brand (proprietary) name may be given more prominence than the proper or common name on drug labels[41] (i.e., beyond what is stipulated within the *Food and Drug Regulations* [C.01.004][18]).
- Graphic elements and "branding" text may interfere with the clear presentation of information that is important to the user.[70] In particular, these aspects of labelling may prevent differences in important information (e.g., strengths, ingredients, indications) from being clearly evident and noted at the time of selection or administration.

Issues can also arise after redesign of a well-known product label. Reasons for a redesign may include standardizing the look of products nationally or internationally,[71] fulfilling marketing purposes, or revising certain aspects of the label to help ensure that errors do not recur. Label redesign requires a balance, such that any existing positive design aspects are maintained for the benefit of users. It has been noted that "while not always feasible, it is important to retest the label designs as they are modified for various purposes, to ensure the changes cause no disruption to the system and user performance."[72]

Recommendations

- Logos and trade dress on product labels should not distract the user or impede the effective communication of key information to the user.[4,8,17,41]
- Strive for balance between the use of corporate trade dress and the presentation of key information on labels. While prominence of trade dress and branding may assist in locating a specific product within the retail environment, it may make it difficult for users to distinguish between different products or different strengths of the same product.[8]
- Consider the amount of space required for a logo and how much space will be available for product information on the remainder of the label.
- Ensure that key information within a product line is clearly differentiated among products to avoid look-alike confusion and the potential for selection error.
- Clearly distinguish different strengths of the same health product or the presentations of different health products by the same manufacturer. Consider the use of colour, together with other elements of the label and package, such as size, shape, or features of the container closure.[8,73]
- When making changes to the label or package, consider user testing before release on the market, to help reduce the potential for unintended consequences (e.g., when rebranding or adding to a product line).[33]

3.3.9 Permanence

Background

The safe labelling of health products ensures that all information is readable for the duration of the shelf-life of the product.[40] It has been noted that important information on product labels may be inadvertently removed with handling and use.[74]

Recommendations

- Ensure that print on products will remain legible for the entire life of the product, taking into consideration transportation and storage conditions, as well as environments of use.[40]
- Consider special technologies, such as smudge-resistant paper stock[75] and inks containing adhesives, which will bond to a variety of surfaces, including plastics.
- Use inks that are resistant to isopropyl or ethyl alcohol and that will be durable enough to withstand normal handling, particularly for injectable products (e.g., ampoules, vials, prefilled syringes).[15,16,35]

3.4 Label information

3.4.1 Key elements on the principal display panel

The principal display panel of a label is the first interface between the user and a health product. It is an important factor in product identification and selection. Health Canada regulations specify information that is required to appear on the principal display panel of a product (*Food and Drug Regulations* C.01.004).[18]

Sponsors are expected to be familiar with the regulatory requirements for their particular product.

In addition to the information required by regulations, eight key elements were identified by the expert advisory panel of healthcare professionals, consumers, and regulators providing input during the development of this guide. These elements assist the user to correctly select a product and use it appropriately. These were noted to be the key pieces of information for inclusion on the principal display panel of health product inner and outer labels (see note below). They align with national and international standards and safety literature, but do not incorporate all of the information required by regulation or guidance for each type of health product. For example, the drug identification number (DIN) is required by regulation, yet is not listed among the eight key elements.

The eight key elements are:

1 brand name of health product
2 non-proprietary name (proper or common name) of health product
3 strength, with or without total amount per total volume
4 dosage form
5 route of administration (other than for oral solids, such as tablets)
6 critical warnings, as relevant
7 population, as relevant (e.g., pediatric)
8 storage instructions, as relevant

Note: It is vital to consider each specific product, its users, the environment(s) of use, and the regulatory requirements to determine which of the eight key elements may be needed to ensure safe use. (Refer to section 3.5.2, "Small Containers and Small-Volume Containers".) For example, oral liquid products may be used in environments such as hospitals or even homes where intravenous access may exist. Because it is possible for any liquid product to be injected,[76] or a suppository to be ingested, it is critical to state the intended route of administration (oral for the liquid, rectal or vaginal for the suppository) on the principal display panel of the label on such products.

For very small containers, the inner label may not have the space to include all of the identified key elements. The nature of the product will then suggest which elements are most critical for safe selection and use and should be included on the inner label taking into consideration the regulatory requirements.

Storage instructions are one of the key elements that are not addressed in a separate section of this guide. It may be relevant to include such instructions on the principal display panel if the typical storage requirement for the product is other than room temperature. For example, products that require refrigeration are less typical, and refrigeration instructions for products requiring low storage temperatures should therefore appear on the principal display panel as an alert to users. This is especially important for vaccines that require refrigeration.

3.4.2 Expression of strength

Background

Expression of strength is a key piece of information on a health product label. Unclear expression of strength, or a missing expression of strength, can impede correct selection and use of products. Individual products may be

available in multiple strengths, and strength may be expressed in a variety of units; as a result, product strengths can be easily misinterpreted.[10]

The following list presents examples of labelling practices that may introduce confusion because of the way in which the strength of a health product is expressed:

- presenting strength in more than one form[10] (e.g., as both a concentration and a percentage)
- using different units of measure on the same label[9] (e.g., millimoles [mmol] and milligrams [mg])
- using different units for volumes[77] (e.g., "per mL", "per mm^3", "per cc")
- presenting a variety of numbers on the principal display panel, such as the strength (in one or more expressions) and the total number of units in the package[8]
- placing the drug strength (a numeric value) and the unit or pack size (another numeric value) in close proximity[9] (refer to section 3.3.3, "Proximity and Compatibility of Information on the Principal Display Panel".)
- mismatching the volume of health product in the container with the expression of strength (e.g., where the entire content of a vial is less than 1 mL, but the strength expression on the label gives the amount of product per millilitre)[8]
- placing more solution in the container than is needed to reconstitute a product[10] or more that is needed to deliver the required dose of a product[79] (i.e., overfilling the container, such that manipulation may be required to withdraw a smaller amount or to remove excess product to prepare the dose to be delivered)
- using trailing zeros (e.g., "2.0", "2.50") or naked decimals (e.g., ".2"); if the decimal point is not correctly perceived, a 10-fold over- or under-dosing error could occur[8,63]
- using certain SI unit abbreviations that are prone to being misread (e.g., for "microgram", the use of "µg" rather than "mcg" may be difficult to discern in some print and size formats and could be misread as "mg"[4])
- inconsistency between the labelled product strength and the "Dosage and Administration" section of the product monograph or the prescribing information.

Other important issues related to the expression of a product's strength may increase the possibility of confusion and error. With regard to health products in the form of a salt, potencies and content of the active component can differ significantly among various salt forms. Therefore, there may be inconsistency in how information is presented and how users refer to (or understand) the strength. Users may find it difficult to distinguish between the dose of an active ingredient's salt form and the dose of the active moiety itself.[80] For example, flupenthixol is available in three salt forms, hydrochloride, acetate, and decanoate. Oral tablets are in the form of the hydrochloride salt. Injectable products are in the form of the acetate salt, where 50 mg provide 42.25 mg of flupenthixol, and the decanoate salt, where 200 mg provide 144.4 mg of flupenthixol. Thus, confusing a dose of 100 mg between the two salts would provide either 72.2 mg or 95.5 mg of the active drug, as well as having a dramatic difference in absorption rates. It is also important to differentiate between two or more formulations of the same active ingredient, especially when the doses differ significantly. Incorrect dosing due to confusion over which formulation was being used (e.g., liposomal vs. conventional amphotericin B) has resulted in serious adverse events, including death.[81]

For health products requiring dilution to achieve a final concentration for use, the strength expressed on the label may differ from what is required for the final product. Unclear dilution instructions have caused medication incidents.[82] The following issues have been observed:

- Product concentration relative to the amount of diluent required for reconstitution can cause confusion, in that the final volume to be administered to a patient may differ from the volume of diluent used.
- Complexity can be added by requiring use of a specific or proprietary diluent or by requiring more than one step—such as reconstitution, followed by dilution—before the product is suitable for administration.
- Dilutions required for pediatric use of a product may differ from those required for adults. Expressions of strength that will aid the user to make appropriate calculations for the more vulnerable pediatric population are therefore important. It is ideal to have commercially available pediatric-specific formulations and concentrations available for administration to children.[83]

Fractional strengths can be more error-prone and confusable, a situation that must be considered when new strengths are added to existing product lines. An example is transdermal fentanyl, which was made available as both 12.5 mcg / h and 125 mcg / h; 10-fold dosing errors have occurred because the decimal point was overlooked.[84] This problem has now been remedied by changing the displayed strength of the 12.5 mcg / h product to read "12 mcg / h". In cases like this one, the decimal point and matching digits can cause confusion; when the drug involved is a high-alert medication, such as an opioid, the effects could be significant.

Dosage forms that release or deliver an amount of product different from the total amount in the container may need careful consideration. An example is a nicotine inhaler, which contains 10 mg per cartridge but delivers only 4 mg. Such a discrepancy may cause confusion for both the prescriber and the user, because of a mismatch between how the prescribed dose is communicated and how the strength is presented on the label. Furthermore, if the available drug is interpreted as 10 mg of nicotine per cartridge, this could also result in a higher dose and an unnecessary step-up of nicotine therapy when converting from the inhaler to a longer acting transdermal nicotine patch.

Recommendations

General Principles
- Express the dose strength of a health product in an appropriate metric system unit,[15,16] except in situations where other units of measure are accepted and required, such as units of potency for biological medicinal products[33] and percentage strength for topical preparations. Numbers without units of measure should not be used to express product strength.
- Use "mcg" rather than "μg" for "micrograms".[63]
  - Health Canada recommends that the abbreviation "mcg" be used.[4] The use of "μg" may be difficult to see in some print and size formats and the Greek letter "μ" might be misread as "m",[4] which can be a contributing factor to dose errors. (Refer to section 3.3.6, "Use of Abbreviations, Symbols and Dose Designations".)
- For numbers with five digits or more, separate the digits into groups of three by a thin space to help prevent misreading (e.g., 1000 mg but 10 000 mg).[65] This format is compatible with both official languages (unlike use of the comma or period) and is the format recommended by the SI system[65] and by Public Works and Government Services Canada.[85]

- Consider spacing between text characters to enhance clarity. For example, leave sufficient space around the slash character ("/") to optimize legibility, given that this character could be misinterpreted as the number "1" (one) or the letter "l" (L).
- Do not use the slash character ("/") to denote the word "or", and avoid its use for separating different pieces of information. Misinterpretation resulting in error has been reported with such uses of this character.[86]
- Avoid the use of trailing zeros (e.g., "2.0", "2.50") and naked decimals (e.g., ".2").[65]
- To the extent possible, ensure consistency between the units expressing the product strength and the units used for dosing instructions.[9]
- Avoid placing expressions of strength near other numeric information, such as the number of units in the package.[8] (Refer to section 3.3.3, "Proximity and Compatibility of Information on the Principal Display Panel".)
- Take older expressions of strength into consideration when comparable products or products of the same class are prepared for market.
  - Changes to expressions of strength, particularly for critical and specialty products, may be problematic. Before changing the expression of strength of a product to different units or a different format, it is recommended to have the new label and package undergo user testing. (Refer to Appendix 2, "Human Factors Principles and Assessment Methods Relevant to Labelling and Packaging".)

Expressing Strength
- Avoid using both metric (SI) units and other units (e.g., milligrams combined with international units)[88] to express the strength of a given ingredient on the principal display panel of the label. Equivalencies may be better expressed and presented on a side or back panel.
- For dosage forms such as transdermal patches, implants, and inhalers or inhalators include the total quantity of the medicinal ingredients (per patch, implant, or inhaler) and the dose delivered per unit of time and the duration of use on both the inner and outer labels.[4]
  - Label the dosage form or delivery unit itself (e.g., patch, implant, cartridge) with the delivery rate of the drug (e.g., "x mg / day").[4]
  - Where the total quantity in the delivery unit does not correspond to the delivered dose, the total amount of drug in the unit may be presented on a side or back panel of the package, rather than on the principal display panel. This is intended to reduce confusion about dosing and to make the information readily available in the event of misuse. (Refer to section 3.5.5, "Transdermal Patches".)

Expressing Concentration
- For liquids intended for oral administration, declare the quantity of each medicinal ingredient per millilitre (e.g., 5 mg / mL)[4,33] or per usual volume to be taken[4,89] (e.g., 25 mg / 5 mL). Products that are intended for use by patients of different ages may best be labelled with the quantity of medicinal ingredient per millilitre. This allows the user to calculate the needed dose across a range of ages, with specific instructions to be provided in the product monograph. Oral dosing devices are important tools to assist in correct dosing. (Refer to subsection "Dosing Devices" in section 2.5.1, "General Packaging Considerations".)

- For small-volume parenteral products (100 mL or less),[90] declare the quantity of each medicinal ingredient per millilitre (e.g., 5 mg / mL), as well as the total amount per total volume (e.g., 20 mg / 4 mL).[4]
  - If the unit volume is 1 mL, there should be only one expression of strength[90] (e.g., 5 mg / mL or 5 mg per mL).
- When the total quantity per total volume is present on the principal display panel of a label, ensure that this information is more prominent than other expressions of strength.[26,90] The total amount per total volume should be the primary expression followed by the strength per mL presented in close proximity.[78,90]
- Use one or more of the techniques described in sections 3.3.1, "Type Style and Size", and 3.3.5, "Colour and Contrast", of this guide (e.g., display the information first, print the information in a larger type size, use bold type, display the information with greater contrast). For example, display "400 mg / 4 mL" more prominently than "100 mg / mL", presenting the less prominent expression within parentheses or in smaller type.
- For products intended as a single dose, in a ready-to-use format (e.g., prefilled syringes), express the strength as the quantity of active ingredient in the volume provided (e.g., 6 mg / 1.2 mL, 4 mg / 0.8 mL). The concentration per mL can be included in the product prescribing information.
- For containers with less than 1 mL total volume, express the strength as the quantity of active ingredient in the volume provided (e.g., 3 mg / 0.5 mL).[90]
- Avoid using percentages to express concentration or strength when usual dosing is based on a weight or volume calculation of the amount to be administered.[14,37] The expression of strength should match the units of measure described in the prescribing information to avoid error.[9]
  - Avoid indicating strength in terms of a percentage or a ratio (e.g., 1:1000)[10,87] to minimize additional calculations that may be required of the user. Exceptions may be health products for which the ingredient strength is included as part of the name (e.g., local anesthetics).[33]
- Epinephrine is one health product for which multiple strength expressions have been used with concentration presented in milligrams per millilitre (mg / mL) or as a ratio (e.g., 1:100 000). For local anesthetics in which epinephrine is a secondary ingredient, the epinephrine component may be expressed as a ratio (e.g., lidocaine 1% and epinephrine 1:100 000). If epinephrine is the only ingredient, the strength should be expressed as "mg / mL"[34] (e.g., 1 mg / mL) and as the total amount in the total volume (e.g., 10 mg / 10mL), as noted in a previous bullet. For large-volume parenteral products, including dialysis solutions, declarations in percentages or in weight per 100 mL (e.g., 1% w/v or 1 g / 100 mL) are considered acceptable, as is the total amount per total volume (e.g., 2.5 g / 250 mL).[4] The total volume in the container should also be stated somewhere on the principal display panel.

Reconstitution and Dilution
- For health products in a liquid form that require dilution before use, include a relevant warning statement (such as "Dilute Before Use") on the principal display panel of both inner and outer labels. Potassium chloride concentrate for parenteral use is one product that requires this warning on the container closure. (Refer to section 3.4.3, "Critical Warnings".)
- For products to be reconstituted or otherwise manipulated (e.g., powders requiring reconstitution for oral or parenteral administration), show the total amount of powder or dry product in the primary container on the principal display panel of both the inner and outer labels. Ensure that this number is

most prominent and that it is not placed close to the expression of final strength. (Refer to section 3.3.3, "Proximity and Compatibility of Information on the Principal Display Panel".)

- For health products in a powder form that require reconstitution followed by dilution before use, include a relevant warning statement (e.g., "Acetazolamide for Injection. Dilute Before Use") on the principal display panel of both inner and outer labels.

Expressions of Strength for Pediatric Products

- For products intended for either adult or pediatric use, present the expression of strength on the principal display panel in a format that simplifies calculation of pediatric doses. Bear in mind that expressions of concentration may need to be applicable to both populations. For example, a product that is normally administered to an adult as a 1 g dose may be administered to a child as a weight-based dose (e.g., milligrams per kilogram [mg / kg]). Thus, if a vial contains 1000 mg in 10 mL (100 mg / mL), it may be better to state the primary strength expression as "1 g / 10 mL" to aid in adult dosing, with the secondary strength expression, 100 mg / mL, facilitating calculation of doses smaller than 1 g.
- For products that require different dilutions for adult and pediatric administration, a warning may be needed on a side panel to indicate the specific dilutions required to produce a ready-to-administer dose for the intended patient population.

Other

- Where different formulations, salts, drug delivery systems, or special conjugates (e.g., antibody-drug conjugates) of the same drug have significantly different dosing regimens, clearly indicate the product type on the label, in close proximity to the strength of the product (e.g., amphotericin B vs. amphotericin B liposome vs. amphotericin B lipid complex, trastuzumab vs. trastuzumab emtansine[91].)

3.4.3 Critical warnings

Background

A critical warning is one that must be highlighted and conveyed to every user before product administration, to facilitate correct product use and to prevent an error that may result in serious harm or death. Critical warnings must attract the attention of users and must create a balance between being explicit yet concise.[54,92] Their goal is to ensure that users notice, read, understand, and comply with the warning message.[93] Critical warning statements are often presented framed or boxed in both the product monograph and patient information leaflets, and are commonly shown on the principal display panel of the inner and outer labels.

The design of the label and package should not convey a conflicting message to users. For example, if a topical medication is provided in a vial similar to that used for injectable products, or an inhalation medication is provided in a capsule format, a warning may not be enough to overcome the user's experience and customary handling and use of similar packages or formats.[94-97] Additional safeguards that consider human limitations, the ways in which users will interact with the product, and the environment in which this interaction occurs will likely need to be incorporated into the product design to help minimize human error.[98,99] A warning added to a label may not be sufficient to alert the user to a critical situation.[100] Ideally, the label and package will align and together will convey the product's intended use.[99] (Refer to section 3.5.1, "General Packaging Considerations".)

Recommendations

General Principles
- Refer to pertinent Health Canada regulations and policies for warning statements and symbol requirements applicable to specific products.
- Ideally, a critical warning should have the following features:
    - It should appear on the principal display panel,[26,45] on both the inner and outer labels. All other warnings should appear on a side or back panel, or a reference should be made to a package insert or patient information leaflet distributed with the product.
    - It should be located in an area where users will have to interact with it in the course of using the product. For multiple-use products, critical warnings should not be located in an area that would be discarded after an initial interaction.[93,101] The most noticeable and effective warnings are placed in such a way that the task is temporarily interrupted and the user must physically interact with the warning before continuing.[54,58]
    - It should be suitable for the intended users, taking into account the knowledge, training, and experience of those who may encounter the warning.[54,58]
- Critical warnings should **not** be
    - broken up by other information (e.g., logos, background text-graphics)[36]
    - placed only on the inside panel of the outer package (e.g., printed on the inside of the box)

Critical Warning Statements
- Use statements that are as brief as possible, with words that are as explicit as possible.[4,92,101-103] Critical warnings provided in this manner are effective in holding the attention of users, align with the principles of plain language, accommodate the requirements of bilingual labelling, and can assist in avoiding clutter on a label.
- Use of a signal word (e.g., "WARNING" or "ALERT") is one component of an effective warning that can help to draw attention to important information.[54,58,101,103]
- If space allows (e.g., on the outer label), consider the following additional components that can help to effectively communicate the warning:
    - a description of the hazard (e.g., "paralyzing agent")
    - the consequence of non-compliance (e.g., "may cause respiratory arrest")
    - the required or desired behaviour (e.g., "patient must be ventilated")[104]
- Use affirmative statements,[33,93] such as "For Intravenous Use Only—Fatal if Given by Any Other Route." Affirmative statements are less prone to confusion than are non-affirmative statements (such as "Not for intrathecal use"), in which the word "not" may be overlooked.[9]

Prominence
- Avoid presenting entire sentences in capital letters or italic type, as these formats are difficult to read.[41,45,58,105]
- Use white space around a critical warning to help emphasize the information.[41,58,92,102]
- Consider a combination of the following features to draw attention to a warning, as the combination may be more effective than any one attribute on its own:[54,93]
    - upper case letters to emphasize signal words[41,45,105]
    - large, bold print[9,10,20,105,106]
    - high contrast

- colour[9,10,105]
- borders[101]
- box frames or keylines[10,102]
- pictorial symbols[107]

- Use colour prudently to bring attention to warnings and to differentiate warnings from other text.[9,41]
  - Particular colour combinations for words and background are associated with each of the three signal words: red background with white lettering for "DANGER", orange background with black lettering for "WARNING", and yellow background with black lettering for "CAUTION".[93,108] Red is typically used to communicate the highest level of hazard, followed by orange and yellow.
  - Consider using red or orange, as these colours have higher hazard-association and may be associated with higher compliance by users.[105] However, there is some controversy about the significance of the colour red, and concerns have been raised that the increased frequency of its use may dilute its effect (e.g., red text has been used on solution bags to warn about the route of administration or other aspects of product use, to highlight medication contents, and to highlight specific electrolyte contents for intravenous replacement and maintenance fluids).[8]

Symbols

- Limit the use of symbols to warnings required by Health Canada and those that have demonstrated effectiveness in enhancing user understanding and product use.[64,103,109] Warning statements can be identified more quickly if they include symbols or pictures that are bold, have high contrast, are simple in form, and closely represent the intended message.[58,104]
- To ensure that these criteria are met, consider user testing of new or unfamiliar symbols, particularly if the product label and package are to be used across cultural groups.[54]

Labels, Caps, and Ferrules

- Critical warnings should be the only information that appears on the top (circle) surface of the ferrule or cap overseal of an injectable product.[90] If information is placed on the side of the ferrule (e.g., numbers or letters representing a lot number or a code number), it must not detract from the warning on the ferrule.[110]
- Other than the critical cautionary statement(s), no other information of any type should appear on the top surface of any ferrule or cap overseal of an injectable product.[110]

Product-Specific Critical Warnings

Ideally, error-prevention strategies such as the use of critical warnings on labels and packaging of a specific product are identified through user testing before they are made available on the market. The following recommendations are based on learning from medication error reporting and analysis from various jurisdictions and organizations. They represent additional improvements identified by regulators, safety organizations and experts, and other stakeholders for inclusion on the main or principal display panels (inner and outer labels) and container, as applicable.

Concentrated injectable medications that must always be diluted before administration

- Ensure that all labels have the following boxed warning: "Concentrate: Must Be Diluted Before Use".[90]

- Caution statements need to be included on the product labels, but can also "appear on the top (circle) surface of the ferrule or cap overseal of a vial containing an injectable product"[90].
- **Potassium chloride concentrate** for parenteral use
  - A black cap or ferrule on potassium chloride vials and one or more black bands above the constriction on an ampoule are restricted to use on potassium chloride for injection concentrate containers.[90]
  - "The cap of the container and the overseal of the cap must be black, and both bear the words: "Must Be Diluted" in readily legible type, in a color that stands out from its background OR the overseal may be of a clear plastic material through which the black cap is visible and the printing is readily legible." [111]

Neuromuscular blocking agents

- Include the following statement on labels, the cap, and the ferrule of all neuromuscular blocking agents: "Warning: Paralyzing Agent" or "Paralyzing Agent".[90,112,113] The warning on the label should be prominently displayed on all principal display panels.
- At a minimum, ensure that the colour of the cap and ferrule and the colour of the print for the warning meets USP requirements:
  - "Both the container cap ferrule and the cap overseal must bear in black or white print (whichever provides the greatest colour contrast with the ferrule or cap colour) the words: 'Warning: Paralyzing Agent' or 'Paralyzing Agent' (depending on the size of the closure system)."[90]
- Consider using a red ferrule with white lettering: "Warning: Paralyzing Agent" or "Paralyzing Agent".[112]
- Consider using a red cap with white lettering: "Warning: Paralyzing Agent" or "Paralyzing Agent".[112] Alternatively, use a clear cap to allow visualization of the ferrule and its printed warning.[90,112]
- Restrict use of a warning in white lettering on a red cap or ferrule (or both) to neuromuscular blocking agents.[112] A red ferrule and cap with the warning in white lettering (or clear cap) is most commonly used for neuromuscular blocking agents available in Canada.[112]
- The use of colour combinations different from what is currently used for neuromuscular blocking agents in Canada (or any other change in the warning for these agents), may require user testing to prevent unintended consequences.[112]
- Refer to ISMP Canada's bulletin on this topic for further information about these recommendations and additional considerations, such as providing a peel-off label for user-labelled syringes.[112]

Vincristine and other vinca alkaloids

- Include the following warning on labels for these products: "For Intravenous Use Only—Fatal if Given by Other Routes".[33,114,115]
- Display the warning prominently on the label.[33,115]

Methotrexate for oral administration

- Ensure that labels for oral methotrexate state the following: "Check dose and frequency—methotrexate is usually taken once a week."[26,33,116]

- Display the warning prominently on the label.[33]

Workplace Hazardous Materials Information System (WHMIS)
WHMIS is a "national hazard communication standard", which specifies the classification of hazardous materials and requirements for the labelling of containers.[117] Some health products may fall under WHMIS regulations and suppliers are required to properly identify and label these products.

3.4.4 Expiry date

Background

Numerous variations exist in how expiry dates are expressed, including differences in the date format, the order of various details, and the grouping of information. These variations may present challenges to users. Incident reviews have shown concerns in two key areas: comprehension and readability.

Issues with Comprehension
- Representation of the year in a 2-digit format has resulted in confusion between the year and the month (e.g., "03-04" may be interpreted as either "March 2004"or "April 2003").[9,10,26]
- Where only the year and month of the expiry date are shown (e.g., "2014-02" for "February 2014"), users, including patients, may not be aware that expiry occurs on the last day of the month.
- Use of a 2-digit format for both the month and the day may lead to confusion between these two elements of the date when the day of the month is 12 or below (e.g., "2015-01-09" may be interpreted as either "January 9, 2015" or "September 1, 2015").
- Where no introductory word or descriptor (e.g., EXP) is included to distinguish the expiry date from the lot number, users may confuse one for the other, particularly if these two details are placed in close proximity or side by side on the product label.[10]

Issues with Readability
- Users may be unable to identify the date because of poor contrast (e.g., black print on a dark background). Embossing, particularly when there is little or no colour contrast, is a related issue that may significantly affect the ability to find and read information on a label.[10,26]
- Problems may arise if the ink lacks permanence.
- Backgrounds that are shiny and reflect light may impede readability.[10]

Recommendations

Enhancing Comprehension
- Include all three components of the date (year, month, day) when applicable and when space permits.[4] Where the expiry date must include the day of the month, use the 4-digit format for the year and express the month using letters (as outlined below).
    - Use hyphens between the three elements (e.g., YYYY-MM-DD for year, month, and day) for added clarity.
    - For the month, use the following abbreviations (which are compatible with both English and French): JA, FE, MR, AL, MA, JN, JL, AU, SE, OC, NO, DE.[4,15,16,40]
      Note: It is possible that "JN" will be mistakenly interpreted as "January" instead of "June";

however, this potential misinterpretation would result in a product being discarded prematurely, rather than being used beyond its expiry date, so carries no health risk. The same would apply if "MA" were interpreted as "March", instead of "May".

  o If the space available on a small container does not permit inclusion of all three components of the date, present the year in a 4-digit form and the month in a 2-letter form, as in the examples below.[4]

- Include a descriptor before the date to alert users to the meaning of the information: e.g., "EXP",[10] "EXPIRATION", "EXPIRATION DATE", "DATE D'EXPIRATION",[4] "EXP DATE", "EXPIRY", "EXPIRY DATE", or "EXPIRES".[89]

Examples:

When all components of the date are applicable:
YYYY-MM-DD: 2024-OC-31
For small containers, if there is space for only the year and the month:
YYYY-MM: 2024-OC

Enhancing Readability

- Separate expiry dates from lot numbers with enough space to prevent confusion and to prevent their being read in combination as a single piece of information. When possible present expiry dates and lot numbers on separate lines.
- Use inks that will not be easily smeared or rubbed off the product or package during normal use (e.g., resistant to alcohol used for disinfection).[15,16,35] (Refer to section 3.3.9, "Permanence".)
- Avoid embossing or debossing of information that results in little or no contrast.[10,35,118] Engraving (i.e., embossing and debossing) of text onto a container may not provide sufficient contrast on its own; therefore, if such methods are used, highlight the text with ink.[16]

Location

- Place the expiry date on the inner and outer labels of all products,[18] in an easy-to-locate area[35]. This can avoid the potential for information to be overlooked. For example, consider placing the expiry date on a side or back panel of the product package.[33]
- Place the expiry date in an area that will not be removed or destroyed when the container is opened.[4,35]
- Refer to section 3.5.4, "Blister Packaging".

Other Considerations

- When labelling a product that contains more than one item with differing expiry dates, use the shortest expiration date on the finished outer product label.

3.4.5 Lot or batch number

Background

Concerns have been described about confusion when a lot number has been misinterpreted as the expiry date or confusion caused by the lot number being combined with the expiry date.[10] Users have also reported difficulty reading the lot number on some labels. Readability is hindered when the text is embossed, when there is a lack

of contrast between the text and the background, and when the printed text lacks permanence.[10,35] For some products (e.g., vaccines), the lot number is a component of the process of verification or documentation by users. In such circumstances, a readable lot number is needed to ensure complete documentation of the product's administration.

Recommendations

Reducing Ambiguity
- Use a term or an indicator word such as "Lot number", "Lot no.", or "Lot" before the lot information to alert the user to this information in the event of a recall.[4,89]
- Separate lot numbers from expiry dates with enough space to prevent confusion and to prevent their being read in combination as a single piece of information. When possible present lot numbers and expiry dates on separate lines.

Enhancing Readability
- Use inks that will not be easily smeared or rubbed off the product or package (e.g., resistant to alcohol used for disinfection).[15,16,35] (Refer to section 3.3.9, "Permanence".)
- Avoid embossing or debossing of information that results in little or no contrast.[10,15,16,35] Engraving (i.e., embossing and debossing) of text onto a container may not provide sufficient contrast on its own; therefore, if such methods are used, highlight the text with ink.[61]

Location
- Place the lot number on the inner and outer labels of all products,[18] in an easy-to-locate area[35]. This can avoid the potential for information to be overlooked. For example, consider placing the lot number on a side or back panel of the product package.[33]
- Avoid placing lot numbers on the top (circle) surface of vial ferrules, in accordance with USP standards.[119]
- Place the lot number in an area that will not be removed or destroyed when the container is opened (e.g., **not** on rip-off tabs or top or neck of ampoules).[9,35]
- Refer to section 3.5.4, "Blister Packaging".

Other Considerations
- When labelling a product that contains more than one item, with each component having its own lot number, a new lot number may be used to represent the combination product.

3.4.6 Automated identification (e.g., bar coding)

Background

Automated identification "is the use of bar codes, radio frequency identification (RFID) and other machine-readable codes to identify, quickly and accurately, an item or process".[120] Although not a mandatory requirement in Canada, automated identification systems offer opportunities to improve the safety and efficiency of health product use at various stages of the product-use process, including procurement, inventory management, storage, preparation, dispensing, and administration.[121] Automated identification systems can also

support product traceability (e.g., during recalls) and verification of the authenticity of health products as they move through the medication-use system.[120]

Recommendations

- Include within automated identifiers the key information necessary to ensure appropriate selection and safe use of the product.[16] The information contained within the automated identifier should not be considered a substitute for providing all required information directly on inner and outer labels.
- Legibility and readability of key information on the label should **not** be impeded by the presence of automated identifiers.
- Information embedded within the automated identifier should not include anything other than approved product information. It should also be focused on the needs of users and be non-promotional in nature.[26] This recommendation applies to any type of automated identifier that appears on the label or package of a health product, including embedded QR (quick response) codes or microchips that can be read with a portable device.
- Information contained within the automated identification must comply with regulatory requirements for health product labelling. Additionally, sponsors must ensure that quality assurance processes are in place, including verification of the accuracy (e.g., the right bar code appearing on the right label) and readability of automated identifiers on health product labels. For automated identification of pharmaceutical products in Canada, consider the information and standards adopted by the Canadian Pharmaceutical Bar Coding Project.[122]

3.5 Packaging

3.5.1 General packaging considerations

Background

Health product packaging is an important factor in promoting the intended and proper use of a product. The type or format of a container often gives users a cue as to the intended route and method of administration.[8] If a health product container, its format, or its appearance looks similar to that of other products intended to be handled differently, errors may occur, and serious harm may result, as in the following examples.

- Providing a topical medication in a vial format similar to that used for injectable medications may lead the user to withdraw the product into a parenteral syringe and then inadvertently inject it.[123,124]
- Providing sterile water for irrigation in a flexible plastic bag may lead users to inadvertently administer it by the intravenous route. The look-alike issues in this situation include presence of an injection port on the sterile water bag and ability to connect intravenous (IV) tubing to the bag.[8]
- Capsules intended for inhalation may be inadvertently swallowed.[95] Conversely, capsules intended to be swallowed may be mixed up with those intended for inhalation.[95]
- Vincristine intended for intravenous infusion may be inadvertently injected intrathecally.[125] Similarly, concentrated potassium chloride intended for dilution and subsequent administration as an infusion may be inadvertently injected without dilution.[126]
- A product intended to treat symptoms of menopause may be mistaken for oral contraceptives, in part because of similarities in package design.[96]

Outer Packaging or Overwrap

The outer packaging or overwrap is a good medium for displaying important information about the product. It may also provide a reliable way of keeping product components together (e.g., drug, dose delivery device, and patient information leaflet).[74] However, caution must be exercised in using this type of packaging, as overwraps, outer packaging, and shipping cartons can also impede the proper identification and use of a product, as in the following examples:

- Reflective material used for the outer label or the overwrap itself may reduce the visibility of key information on the label.[35]
- Products may be stored in poorly labelled shipping boxes, which may contribute to misidentification and selection errors.[35,126]

Multi-Part Products

Health products consisting of multiple items (e.g., a vaccine and its diluent) to be used together can be packaged such that all components are provided in one package; alternatively, the items may be packaged separately. Errors can occur when the labelling or packaging does not support correct use of the separate components by the user, as in the following examples:

- poor labelling not clearly indicating that the product has multiple components and that all must be used together[127,128]
- poor visibility of one of the components (e.g., obscured or not clearly visible or accessible) in the combined package, leading the user to assume that only the visible component is required (e.g., the diluent for a product requiring reconstitution was provided in a prefilled syringe, which was mistaken for a ready-to-use product; as a result, the active drug was not reconstituted, and only the diluent was administered[127])
- lack of prominence of key information for product-specific diluents[127]

Dose Delivery Devices

Health products intended for the pediatric population are often provided as oral liquid formulations for ease of administration.[129] Some of these products are packaged with a measuring or dose delivery device intended to assist with the administration of a specific volume or dose by the patient. This presentation of the oral dose delivery device is intended to give users a way to accurately prepare and administer the dose.[33]

Recommendations

General
- A number of factors can be considered when choosing a package. These include maintenance of product stability, ease of manufacturing, choice of distribution system, product security, ease of use, and even user compliance.[130]
- Provide health products in a container that facilitates correct selection and use, rather than relying only on labelling features such as warnings. Well-designed packaging can help to minimize the risk of medication errors.[130]

- Consider how the product will be used at the point of administration. For example, if the product will be administered intravenously, design the package and label such that the information is oriented for optimal readability when the container is hung on an IV pole.[130]
- When a completely new type of container is being considered for a health product, with no market experience to draw upon, consider user testing as part of product development.[81] This is especially important when a new type of container is used for an existing product.
- If space permits, consider providing additional cues to assist the user in identifying, selecting, and using the product (e.g., use the international chemical symbol "H_2O" on bags of sterile water; use a unique size and shape of container for a particular product).[10,99]

Outer Packaging or Overwrap
- To improve the visibility of key information, avoid using reflective materials for overwrap (e.g., overwrap for intravenous solutions); use matte materials whenever possible.[35]
- Consider printing and highlighting critical product information on shipping cartons for products that may be stored in the original shipping carton. In this situation, the information should be printed on at least three non-opposing faces of the carton.[4,35]

Multi-Part Products
- Whenever possible, avoid separately packaging the different components of a multi-part product. Instead, provide and package together all components of the product that must be used to prepare and administer the dose.[127]
- Create a package that, when opened, allows clear visualization of (1) all co-packaged products intended to be used concurrently, and (2) instructions for combining them. Ensure that the labels clearly identify the number of parts and how they must be combined and used.[4,81]
- To prevent dilution errors, when supplying a diluent, provide it in the exact volume needed for reconstitution.[131,132]
- Each component of co-packaged products that are intended to be used separately (e.g., day and night prenatal vitamins) should be packaged in separate immediate containers (e.g., blisters).

Dose Delivery Devices
- Include dose delivery devices with all liquid health products intended for oral ingestion, with dose information expressed in units of measure corresponding to the calibration of the dose delivery device.[133-135] (Refer to section 3.5.3, "Pediatric Products".)
- The dose delivery device should have a marking for the smallest recommended single dose to allow measurement of such a dose.[133,134]
- The dose delivery devices should **not** be significantly larger than the largest single dose recommended on the product label.[134]
- A dosing device should be recalibrated when changes are made to the strength of the product with which it is intended to be used.
- Provide clear and specific instructions on how to measure and administer a precise dose. The addition of drawings showing time, method, and route of administration may be helpful for some users.[136] Drawings should undergo user comprehension testing.
- Use SI and metric units for measurements on oral dose delivery devices and other label information.[9,65,137]

- Use sufficient colour contrast for graduations or markings on dose delivery devices, to prevent the markings being obscured when the liquid product is added to the device.[134] For example, use black ink on a white field of view.[15]
- Avoid the use of trailing zeros after decimal points ("2" not "2.0") to help avoid 10-fold dosing errors.[63,132]
- Use leading zeroes before decimal points ("0.2" not ".2") to help avoid 10-fold dosing errors.[63,132]
- To prevent inadvertent parenteral administration of liquids intended for oral use, an oral applicator (e.g., oral syringe) provided as a dose delivery device should not accommodate a needle.[138]
- Ensure that container caps used as dose delivery devices for oral liquids are of adequate size and design to not pose a choking hazard to children.[138]
- For oral liquid preparations that have a narrow therapeutic window or that require dosing volumes less than 5 mL, spoons or cups are not considered acceptable.[138]

3.5.2 Small containers and small-volume containers

Background

The terms "small container" and "small-volume container" are reserved for containers with obvious restrictions on the amount of information that can appear on the product label or package.[46,141] This includes special containers that are too small to accommodate a full label.[4]

The use of small containers may give rise to errors because of difficulties in reading or understanding labels on the product, as in the following examples:

- lack of information about the product (e.g., absence of total dose, strength, or concentration of active ingredient, absence of reconstitution instructions)[8]
- inability to easily identify vials and ampoules containing concentrated solutions of medication that must be diluted before parenteral administration[139]
- orientation of text whereby the field of view is limited by curvature of the small container (e.g., similar names of products provided in ampoules may be more easily confused if product names are printed horizontally around the circumference of the ampoule, rather than along its long axis, especially for smaller ampoule sizes of 1, 2, and 5 mL[35])

Recommendations

- Consider container size and label design in the early stages of product development.
- Consider any container not large enough to accommodate an inner label complying with C.01.004(1) of the *Food and Drug Regulations*[18] to be a small or small-volume container, for which these recommendations should apply.
- Discuss with Health Canada the determination of what is acceptable as a small or small-volume container before submission of product application and as early as possible during the product development stages.
- Reserve the use of small or small-volume containers for situations where their use does not negatively influence the product's safety profile. For example, the safety benefits of providing an injectable

medicine in a small volume (to limit the total amount in each container to a single dose) may outweigh the potential problems of the smaller inner label.

- To enhance readability of key information by users, consider the size and orientation of text on small containers.[35] The orientation of text should be the same as the field of view so that it is not limited by physical aspects of the small container, such as curvature.
- Consider using a larger container, larger labels, or innovative package and label designs when space is limited (e.g., use larger containers than required to accommodate the total volume of eye drops or tablets or use tag, fold-out, or peel-back labels). Novel label formats should comply with applicable regulations and guidance documents.[1,4] For the labelling of drug ampoules, vials, and prefilled syringes, consider information provided in the CSA standard Labelling of Drug Ampoules, Vials and Prefilled Syringes.[15]

3.5.3 Pediatric products

Background

The pediatric population is inherently at high risk of harm from medication errors.[133] The number of preventable medication errors in this population is three times higher than among adults being treated in hospital.[142] When an error does occur, infants and children are at greater risk of harm or death from an error than are adults.[143] The following labelling and packaging factors can put the pediatric population at increased risk:

- requirement for individualized dose calculations based on age, weight (e.g., mg / kg), or body surface area[133]
- misinterpretation of labels or of markings on dose delivery devices, leading to under- or over-dosing[135]

Recommendations

- If a pediatric formulation is significantly different from a similar adult product, consider making the labelling and packaging noticeably different for the two products.[136]
- Design product packaging and container closures to prevent or limit children from accessing the contents.[130]
- If appropriate, separate bilingual information to prevent any misinterpretation of details about pediatric products intended for children but **not** infants. For example, in French, the word "enfants" means "children", but this word differs by only one letter from the English word "infants".
- Provide clear and specific instructions on how to measure and administer a precise dose. The addition of drawings showing time, method, and route of administration may be helpful for some users. Drawings and graphics should undergo comprehension testing. (Refer to Appendix 2, "Human Factors Principles and Assessment Methods Relevant to Labelling and Packaging".)
- If a measuring or dosing device is supplied with liquid formulations of products intended for pediatric use, the instructions provided should be consistent with the measuring device.[144]

3.5.4 Blister packaging

Background

Blister packs can be manufactured in a number of configurations, including individual blister cells in a strip that is perforated to allow separation as unit doses or a sheet containing multiple doses to be used as needed or intended for a particular duration of therapy (e.g., 3 days, 2 weeks, 1 month).[9] A blister pack can be removed from its outer package, cut into smaller units, or torn along perforations. Such actions can leave the product information unclear or unavailable, thus jeopardizing safe use of the product. The following concerns have been raised about the design of blister packs:

- illegibility of drug name or strength, for reasons such as use of reflective foil and lack of contrast between type and background[8,9,26,41,46]
- inability to identify drug name or strength of remaining tablets, capsules or lozenges after some have been removed from the blister pack[8,41]
- printing of the product name and strength across two blister cells, making it unclear whether labelled strength is provided by the contents of two cells or just one[8,70]
- mismatch between display of information and perforations on a blister pack[80]
- reduced ability to identify the product once the blister pack has been removed from the outer packaging or box (i.e., difficulty matching the blister pack with the outer box[41]), a particular problem for consumers who have more than one health product packaged in this format
- difficulty removing the product from blister packs[145]
- presentation and sequencing of doses in ways that do not match the product's approved usual dosage:[9,146]
    - labelling of doses with days of the week, when such labelling is not required[9]
    - numbering of blister cells in sequence[9]
    - provision of more doses than needed for a usual single course of treatment[9]

Recommendations

General
- Select a blister material that will not impair legibility of key information on the blister cell. For example, foils may be unsuitable for this purpose, as their reflective nature can reduce the legibility of printed information.[26,41]
- Provide the following information on each blister cell:
    - proprietary (brand) name (or product name, if there is no brand name)
    - established (common, proper) name or, for a drug with more than one medicinal ingredient, the brand name of the drug or health product
    - strength of the health product, except where the name used is unique for a particular strength of the product (e.g., for a product with more than one medicinal ingredient)
    - route of administration (other than for oral solids such as tablets)
    - lot number
    - expiry date
- If information cannot be placed on each blister without becoming illegible, present it in a way that prevents the drug or product name (brand name at a minimum) and strength from being detached or

destroyed when any dosage unit is removed. For example, consider repetitive diagonal[26] or random display[9]. It may be acceptable to place the lot number and expiry date on one end or both ends of the blister strip.[26]

- Avoid perforations, if separation of blister cells along these perforations will inappropriately break up certain information (e.g., brand name and strength).
- Design the blister pack to be consistent with product information and instructions for use:[9]
    - o Avoid placing product information directly across two blister cells, to prevent the user from thinking that two tablets or capsules are equivalent to the dose actually provided in one tablet or capsule.[8,146]
    - o Include only one dosage unit (e.g., one tablet, one capsule, one lozenge) in each blister cell.[9] If multiple dose units are indicated to be taken as a single dose, this should be specified in the dosing instructions.
    - o If perforations are used between blister cells, they should allow for separation of each individual blister from the original pack.[8] Perforations which include more than one blister cell may indicate dosing different to that intended (e.g., two cells within a perforated unit, rather than one, could be interpreted as the contents of two cells are to be taken per dose).
    - o Consider use of new technologies where the inner label adheres to the blister pack, so that key information remains for the duration of product use.
- In circumstances where the label could become detached during use, print key information on each blister cell.

Health Products Intended for Sequential Use (e.g., Oral Contraceptives)
- Avoid perforations on this type of blister format, as the medicine or product is intended to be taken in a specific order, and individual blisters may contain different products and product doses.
- Ensure that the legibility of the required information on the blister pack is not affected as doses are removed.[4] For example, required information may be placed in a single location that is not removed or destroyed for the duration of product use.
- Expiry Date and Lot Number:
    - o Ideally, print the expiry date and lot number over each blister, so that they are still legible when only the last dose remains, especially if individual blisters are detachable.
    - o Place the expiry date and lot number in a single location on "race-track" blister packs (e.g., oral contraceptives), such that they will not be torn during use (e.g., on the heat-sealed end of the package).
    - o Place the expiry date and lot number so that they are aligned between perforations, if present (i.e., printed on areas between perforations, so that the information will not be lost when individual blisters are torn away).

3.5.5 Transdermal patches

Background

The use of transdermal medications and the properties unique to this delivery system have led to errors resulting in poor patient outcomes.[147] The following general issues have been reported with the use of transdermal patches:

- Transdermal patches manufactured from a clear translucent or skin-coloured material (to make them less conspicuous when in use[147]) can make it difficult to see a patch on the skin. There is a possibility of overdose if patients or their caregivers cannot visually identify an existing patch and a second patch is applied without removing the first one. Poor patch visibility can also lead to unintended drug exposure if a caregiver, child, or pet comes into contact with a patch that has fallen off or has been improperly discarded.[73] This safety risk is of particular concern with high-alert medications (e.g., fentanyl).[148]
- Key information, such as the drug name and strength, should be clearly presented on the patch itself. This provision is especially important for patients who are unable to communicate their medication use and for caregivers and healthcare professionals who are unfamiliar with or have not had previous contact with the patient (e.g., emergency department staff at a hospital, emergency medical services staff). Healthcare professionals must be able to identify the contents of a patch so they can take appropriate measures with regard to that therapy (e.g., pain management, blood pressure control, smoking cessation) or potentially contraindicated therapy.[149]

Recommendations

The recommendations presented here are important for any transdermal format and are especially critical for medications where severe harm could result if the patch is not seen after it is applied or if the patch falls off. Significant safety risks are associated with making patches invisible or too discrete.

- Ensure that the information required on transdermal patches is visible and legible and that the ink is long-lasting.[150]
- For any text on a transdermal patch, use a colour that will ensure visibility of the patch when applied to the skin.[148,150]
- Consider using a colour for transdermal patches that will further increase their visibility when applied[148] regardless of the patient's skin tone. "Clear or translucent patches may also be difficult to find if they detach prematurely from a patient; thereby increasing the potential for secondary or accidental exposure" to the drug.[73]
- Based on findings from incident reports, the following information should appear on a transdermal patch:
  - brand name
  - proper or common name
  - delivery rate of the drug (e.g., "X mg / hour")

Appendix 1 - Glossary

Active ingredient: "means a drug that, when used as a raw material in the fabrication of a drug in dosage form, provides its intended effect." (*Food and Drug Regulations*, Section C.01A.001[18])

Aggregate analysis: see "Multi-incident analysis"

Brand name (Drug): "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" (*Food and Drug Regulations*, Section C.01.001[18])

Close proximity: "means, with reference to common name, immediately adjacent to the common name without any intervening printed, written or graphic matter" (*Food and Drug Regulations*, Section B.01.001[18])

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*" (*Food and Drug Regulations*, Section C.01.001[18])

Confirmation bias: a phenomenon that "leads an individual to 'see' information that confirms their expectations, rather than to see information that contradicts expectations." (Human factors and substitution errors. ISMP Can Saf Bull. 2003;3(5):1-2.[180])

Critical incident: "an incident resulting in serious harm (loss of life, limb, or vital organ) to the patient, or the significant risk thereof. Incidents are considered critical when there is an evident need for immediate investigation and response. The investigation is designed to identify contributing factors and the response includes actions to reduce the likelihood of recurrence." (Davies J, et al. Canadian Patient Safety Dictionary. 2003[152])

Critical Warning: A critical warning is one that must be highlighted and conveyed to every user before product administration, to facilitate correct product use and to prevent an error that may result in serious harm or death.

Drug: "includes any substance or mixture of substance**s** 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 functions in human beings or animals, or
(c) disinfection in premises in which food is manufactured, prepared or kept;" (*Food and Drugs Act*, Section 2[5])

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." (*Food and Drug Regulations*, Subsection C.01.005(3)[18])

Expiration date or Expiry 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." (*Food and Drug Regulations*, Section C.01.001[18])

Font: "A complete set of characters in one design, size, and style. In traditional metal type, a font meant a particular size and style; in digital typography a font can output multiple sizes and even altered styles of a typeface design." (Carter R, et al. Typographic design: Form and communication, fifth edition. 2012[12])

High-alert medications: "drugs that bear a heightened risk of causing significant patient harm when used in error." (Institute for Safe Medication Practices. c2015.[153])

Human factors engineering: "the discipline concerned with understanding how humans interact with the world around them. It draws upon applied research in many areas, such as biomechanics, kinesiology, physiology, and cognitive science, to define the parameters and restraints that influence human performance. This knowledge can be used to design systems so that they are compatible with human characteristics. Conversely, if systems are not compatible with human characteristics, performance can be adversely affected." (Institute for Safe Medication Practices Canada. Failure mode and effects analysis (FMEA): A framework for proactively identifying risk in healthcare. Version 1. 2006[151])

Immediate container: "means the receptacle that is in direct contact with a drug" (*Food and Drug Regulations*, Section C.01.001[18])

Inner label: "means the label on or affixed to an immediate container of a food or drug" (*Food and Drug Regulations*, Section A.01.010[18])

Key Elements: For the purposes of this guide, eight elements were identified by the expert advisory panel as being the key pieces of information for inclusion on the principal display panel of a health product label. These elements assist the user to correctly select a product and use it appropriately. They are intended to complement international regulatory recommendations and align with national and international standards and safety literature. They do not incorporate all of the elements required by regulation or guidance for various types of health products. For example, the drug identification number (DIN) is required by regulation, but is not listed among the eight key elements.

Key Information: For the purposes of this guide, key information includes the key elements (refer to section 3.4.1, "Key Elements on the Principal Display Panel" for further information) and label information required by regulations.

Label: "includes any legend, word or mark attached to, included in, belonging to or accompanying any food, drug, cosmetic, device or package" (*Food and Drugs Act*, Section 2[5])

Legibility: Ease of identifying each letter or character; affects the readability of words and sentences.

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" (*Food and Drug Regulations*, Section A.01.010[18])

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" (*Food and Drug Regulations*, Section A.01.010[18])

Medication error: see "Medication incident"

Medication incident: "Any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the healthcare professional, patient, or consumer. Medication incidents may be related to professional practice, drug products, procedures, and systems, and include prescribing, order communication, product labelling/packaging/nomenclature, compounding, dispensing, distribution, administration, education, monitoring, and use." (Institute for Safe Medication Practices Canada. Definitions of terms.[154]).

Microgram: one-millionth of a gram, 1×10^{-6} gram.

Mock-up: In the context of medication labelling and packaging, a full-colour, actual-size copy of the labels and a colour representation (e.g., photograph) of the packages **intended to be used for the sale of the drug**, including all presentation and design elements, proposed graphics, fonts, colours, and text (with a place holder for expiry date, DIN, and lot number).

Multi-incident analysis: "a method for reviewing several incidents at once instead of one by one, by grouping them in themes (in terms of composition or origin) … This method of analysis can generate valuable organizational and/or system-wide learning that cannot be obtained through the other methods." (Canadian Incident Analysis Framework. 2012[155])

Non-proprietary name: describes the drug substance. International Non-proprietary Names are unique, universally applicable, and globally accepted names. A non-proprietary name is the proper name of an ingredient (or the common name if the ingredient has no proper name). (*Food and Drug Regulations*, Section C.01.001[18])

Outer label (Drug): "means the label on or affixed to the outside of a package of a food or drug" (*Food and Drug Regulations*, Section A.01.010[18])

Package: "includes anything in which any food, drug, cosmetic or device is wholly or partly contained, placed or packed" *(Food and Drugs Act*, Section 2[5])

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" (*Food and Drug Regulations*, Section C.01.001[18])

Plain Language: "is a clear writing style designed to be easy to read and understood by the intended audience. It includes how information is organized and displayed within a space, such as the use of white space, fonts, 'active' instead of 'passive' voice of instructions, design elements and color. (Guidance Document: Questions and Answers: Plain Language Labelling Regulations[156])

Point: "A measure of size used principally in typesetting … It is most often used to indicate the size of type or amount of leading added between lines." (Carter R, et al. Typographic design: Form and communication, fifth edition. 2012[12])

Point size: "the approximate distance from the top of an uppercase letter to the bottom of a lowercase letter with a descender (for example, the bottom of a 'j')." (Singer JP, et al. Manufacturer's guide to developing consumer product instructions. 2003[157])

Principal display panel (also referred to as "main 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." (*Consumer Packaging and Labelling Regulations*, Section 2[158])

Proper name (Drug): "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 in any of the publications mentioned in Schedule B to the Act in the case of drugs not included in paragraph (a), (b) or (c)" (*Food and Drug Regulations*, Section C.01.001[18])

Proprietary name: see "Brand name"

Readability: "Readability refers to how easy a piece of writing is to read and understand." (Plain Language Commission. Readability Reports[159])

Root cause analysis: "an analytic tool that can be used to perform a comprehensive, system-based review of critical incidents. It includes the identification of the root and contributory factors, determination of risk reduction strategies, and development of action plans along with measurement strategies to evaluate the effectiveness of the plans." (Canadian Patient Safety Institute. Canadian Root Cause Analysis Framework. 2006[160])

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." (*Food and Drug Regulations*, section A.01.010[18])

Substitution error: an error where the wrong product is selected instead of the intended product.

Le Système international d'unités (The International system of units, also known as the "SI"): "consists of a set of base units, prefixes and derived units…:
- The SI base units are a choice of seven well-defined units which by convention are regarded as dimensionally independent: the metre, the kilogram, the second, the ampere, the kelvin, the mole, and the candela.
- Derived units are formed by combining the base units according to the algebraic relations linking the corresponding quantities. The names and symbols of some of the units thus formed can be replaced by special names and symbols which can themselves be used to form expressions and symbols of other derived units.

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The SI is not static but evolves to match the world's increasingly demanding requirements for measurement."
(Bureau International des Poids et Mesures. The International System of Units (SI), 8th edition. 2006.[65])

TALLman lettering: the application of upper case lettering to certain syllables or groups of letters within look-alike, sound-alike names as a method to assist in their differentiation.[22] This technique should be specifically applied to non-proprietary (proper or common) drug names. In order to demonstrate the concept of using capital letters within a word, "TALLman" is used in this guide.

Trade dress: "any material quality of a product's packaging or physical appearance that serves a branding function."[161] This includes "the manner in which a company packages, wraps, labels, a drug or biologic product including the use of colour schemes, sizes, designs, shapes, and placements of words or graphics on a container label and/or carton labeling."[9]

Type size: is commonly measured in points. See "Point" and "Point size".

User: group or individual who will use a health product in the sponsor's original container with its original label. Users can be identified through product use mapping and can include a sponsor's internal staff as well as users across the supply chain, including the point of administration of a health product.

White Space: "the 'negative' area surrounding a letterform" (Carter R, et al. Typographic design: Form and communication, fifth edition. 2012[12]). Such white space on a product label or package refers to any space not covered by print, markings, coloured graphics, watermarks, or other elements of the label

Appendix 2 - Human Factors Principles and Assessment Methods Relevant to Labelling and Packaging

Human Factors: An Overview

Human factors engineering is a discipline concerned with understanding human characteristics and how humans interact with the world around them.[154] These characteristics and interactions can be referred to as "human factors". The discipline draws upon applied research in many areas (e.g., cognitive science, physiology, kinesiology, biomechanics) to define the things that influence human performance. This knowledge can then be used to design processes, systems, or objects that humans use or interact with so that performance is enhanced and errors are minimized.

It is important that product labels and packages be designed with the user in mind and with consideration of the environment and processes in which the product will be used (stocked, selected, and administered). Users are not designers, and designers are not users.[162] Although it is the designers who are primarily responsible for the design process, consideration should be given to involving users in all aspects of product design from the outset. In particular, designers must go beyond simply asking users what they may need or want.

Label and package designs may also benefit from ongoing review, also known as iterative design[163] Making stepwise changes to a label or package design and tracking the rationale for each design change can help to optimize the design process. Part of the process can include asking the following questions. Is the information on the label grouped in a manner that will be understood by the user? What information is most prominent? What does the container tell the user about how the product is to be used? Does the product's appearance and how the information is presented infer the appropriate meaning to the user?

The following subsections present sample questions that can be used to define users and environments of use.

Users

Most products will have multiple types of users with different visual acuity, underlying diseases or conditions, and the number of health products already being used. Each category of user will have different requirements. To optimize safety, label and package design features may need to accommodate these differing requirements. Ideally, testing should involve novice users (people with little to no experience or knowledge of the product), occasional users (people with limited previous experience, who may not recall details of previous use), transfer users (people whose previous experience involves only similar health products, not the product in question), and expert users (people with extensive experience and knowledge of the product under consideration).[164]

- Will the product be used by patients with or without help from healthcare professionals?
- Which healthcare professionals, if any, will be involved in using the product (e.g., naturopathic doctors, nurses, pharmacists, physicians, respiratory therapists)?
- What age groups of patients are expected to interact with the health product?
- Should problems with vision (e.g., partial sightedness, deficiencies in colour perception) be considered in product design? Visual capacity may be particularly relevant for products intended to treat eye problems or support eye care, as well as for products for conditions in which vision may be compromised (e.g., diabetes

mellitus). Computer software can be used to process digital images of health product labels and packages to simulate the effects of common colour deficiencies.

- How knowledgeable is the typical user (e.g., doctor, nurse, technician, caregiver, patient)?
- What characteristics might the users have that could affect their ability to use the product correctly (e.g., physical strength, dexterity, coordination, vision, hearing, memory, disease state, mental clarity, ability to swallow, tolerance of medications that are unpalatable or are difficult to swallow or ingest)?
- How simple or complex is it to use the product, i.e., are multiple steps or excessive manipulation needed to use the product?
- What critical tasks are users expected to perform simultaneously?

Environments of Use

Health products may be used in hospitals, long-term care facilities, healthcare professionals' offices, dialysis centres, other free-standing care centres, retail pharmacies, dispensaries, specialty pharmacies, emergency transport settings, and the patient's home. Although all interactions with health product labels and packages will ideally occur in optimal environments, health products are often used and stored in poorly lit rooms with multiple high stress variables contributing to the complexity of choosing and using a product.

- What are all the possible environments where users may interact with the health product?
- Are similar products already being used within these environments? If so, is their mode of use similar to that of the proposed product?
- Have there been errors with similar products in the environment?
- What is the expected lighting level in locations where the product is likely to be selected and used?
- Could the choice of colours and contrast negatively impact the ability to select and use a product in low-light environments?
- Where is the product stored?
- Is the product typically stored in multiple locations?
- What other types of products may be stored in close proximity?
- How is the product stored? Does the way it is stored affect the orientation of the label?
- Are there storage limitations (e.g., temperature stability, light sensitivity)? If so, could they affect how the product is stored?
- How busy or distracting is the environment?
- Is the user expected to perform other tasks while interacting with the product?
- What tools and technologies (e.g., automatic dispensing cabinets, medication administration records, bar-coding technology) are already in use in the environment, and will the design of the proposed health product be suitable?

Any form of assessment, whether internal or external, requires a good understanding of who the users are, how the product will be used, the environments in which it will be used, and how users will interact with various aspects of the product, such as the container, the inner and outer labels, the packaging itself, and dosing devices.

User Testing

What Is User Testing?
User testing refers to a broad set of methods for assessing usability, identifying problems experienced by users, and developing solutions to eliminate or reduce the consequences of these problems. User testing simulates or mimics the circumstances of product use to provide a realistic view of how the label and package function within the intended environments. User testing is not quality assurance testing, nor is it market research. User testing is performed under controlled conditions to determine whether people can accomplish specific goals with the product or system of interest.

How Can User Testing Help?
User testing can help to determine whether the intended users can safely and effectively perform the critical tasks involved in selecting and using the health product or whether they will make errors, have difficulty, or be unable to use the product at all. This is especially important for high-alert products.

User testing can be used to discover more specific information about users' experiences with a product and can help to identify problems beyond the general principles outlined in this guide.

When Should User Testing Be Considered?
Although not mandatory, sponsors are encouraged to consider user testing in label and package design in the following situations:

- new label or package design (e.g., design that is novel or not normally associated with the product)
- additions to a product line (e.g., addition of an extended-release formulation)
- changes to a currently marketed product (e.g., new packaging configuration, new indication of use, new delivery system, new target population)
- significant changes to layout or colour of a label (e.g., changes that may affect readability or reorganization of key information)
- change in drug status (e.g., from prescription to non-prescription)critical safety issues (e.g., fatal if given by the wrong route of administration)
- post market safety issues with the product label or package

User testing carries certain costs, however these up-front investments are often much lower than the economic costs of correcting poorly designed packages and labels that increase the risk of serious harm after the products have been released on the market. Well-designed packages and labels improve user satisfaction and can ultimately cost less for a wide variety of reasons.

User Testing Methods

Information and links are provided below to a number of methodologies that may be used to assess labels and packages. With higher levels of risk, additional and more rigorous testing methods are typically recommended. Development of product-use process maps are an integral component of these methodologies.

Failure Mode and Effects Analysis[73,151]

Failure Mode and Effects Analysis (FMEA) is a type of proactive risk assessment that can be used to systematically evaluate product-related hazards and points of risk within the broader system where a product will be used (users, environments). It represents a way to identify and prioritize these risks, identify strategies to mitigate or address problems or potential errors (e.g., to reduce the probability of occurrence of the error, to reduce the severity of consequences of an error, or to increase the likelihood that the error will be noticed), and evaluate the mitigation strategies.

Comprehension Testing[74,165-169]

Comprehension testing assesses user understanding of the communication elements of a label based on language, layout and graphics.[170] It should ideally be applied to all key messages on product labels.[74] Comprehension testing involves having an interviewer show the health product or a mock-up to participants and asking them to state the meaning of the label's content (e.g., abbreviation). The interviewer then asks additional questions to assess any discrepancies between intended and interpreted meanings and to identify potential solutions to these discrepancies.

Cognitive Walkthrough[151,171-173]

Cognitive walkthrough involves guiding a small number of users through a process or task, often early in the design process, to examine mental activities and challenges experienced.[171,172] It can be used as part of an FMEA and can be applied in any setting.[151] Cognitive walkthrough can be used to assess health products that have a narrow therapeutic index, those that are contraindicated in specific populations, and to assess critical warning messages.

Users walk through the assigned tasks, "thinking out loud" as they do so, to allow the investigator to gain a detailed understanding of users' expectations and challenges. Potential design solutions identified through the cognitive walkthrough should then be applied to improve the design of health product labels and packages.

An accurate understanding of the situation, achieved by involving users in their own environments (either real life or "high-fidelity simulations"), will enhance the value and benefit of findings of the cognitive walkthrough.

Usability Evaluation

Usability evaluation (also called simulated-use testing or user testing) is a systematic way of collecting data from representative participants in realistic situations. It involves having users perform specific tasks as part of a scenario while data are collected to identify potential errors or challenges. Similar to the scenarios for a cognitive walkthrough, the scenarios for usability evaluation provide context. A set of tasks is then assigned to be performed by participants. Scenarios are developed on the basis of user consultation, the product-use process map, and direct observation.

User testing can include cognitive walkthroughs with enactment of scenarios that replicate as closely as possible the real product-use process, or components of that process. Verbal protocol analysis can be used, whereby participants are instructed to think aloud during the scenarios and vocalize all thoughts and difficulties encountered.[174] Information collected can include user feedback (e.g., satisfaction surveys, interviews), task analysis (e.g., number of steps in the process), and task performance measures (e.g., training time, completion time, number of steps that cause confusion, number and nature of errors made by users).

Experiment: Memory Tasks[175-177]

Information recall tasks can be performed to assess how label design affects a participant's memory of information presented on the label. Experiments involving memory tasks can be used to assess labels and packages of products with a risk of severe harm or death if administered in error or given by the wrong route, as can occur with high-alert medications.

Experiment: Selection Tasks

Health product selection tasks can be used to assess or compare performance as affected by label or package design. This method has been used to compare existing labels against redesigned drug labels,[178] to assess the comprehension of common abbreviations,[179] and to determine whether inclusion of an additional sponsor logo will affect drug selection.[72]
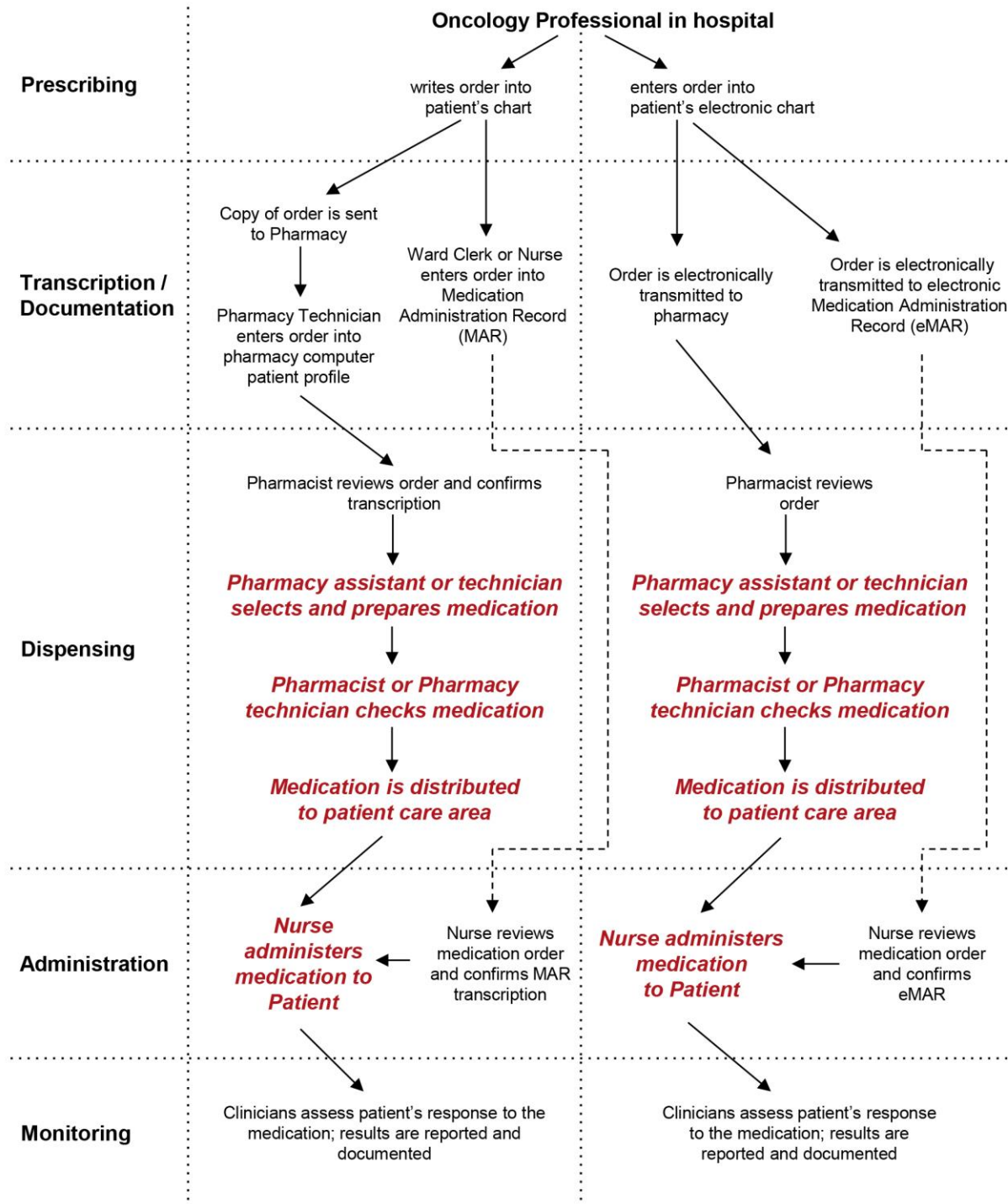
Appendix 3 - Product-Use Process Maps

Product-use process maps outline where and how a product will be used, according to its indications and who will potentially come into contact with it. They are intended to provide a complete and accurate understanding of how the product will be used, the environments of use, and how users will interact with it (e.g., with the container closure, container label, packaging and package labels, dose delivery devices) to identify and make decisions about using the product.

Product-use process maps can be helpful when human factors-based user testing is planned, as such maps will help in identifying the scope of use and the primary users.

An example of a product-use process map is presented below. Selection and administration are the key points in the process where users interact with products (specifically with the label and the package). In the example below, these points of interaction are presented in red italic text.

Sample Medication-Use Process Map for an Intravenous Antineoplastic Drug

Oncology Professional in hospital

Prescribing
- writes order into patient's chart
- enters order into patient's electronic chart

Transcription / Documentation
- Copy of order is sent to Pharmacy → Pharmacy Technician enters order into pharmacy computer patient profile
- Ward Clerk or Nurse enters order into Medication Administration Record (MAR)
- Order is electronically transmitted to pharmacy
- Order is electronically transmitted to electronic Medication Administration Record (eMAR)

Pharmacist reviews order and confirms transcription

Pharmacist reviews order

Dispensing
- *Pharmacy assistant or technician selects and prepares medication*
- *Pharmacist or Pharmacy technician checks medication*
- *Medication is distributed to patient care area*

- *Pharmacy assistant or technician selects and prepares medication*
- *Pharmacist or Pharmacy technician checks medication*
- *Medication is distributed to patient care area*

Administration
- *Nurse administers medication to Patient*
- Nurse reviews medication order and confirms MAR transcription
- *Nurse administers medication to Patient*
- Nurse reviews medication order and confirms eMAR

Monitoring
- Clinicians assess patient's response to the medication; results are reported and documented
- Clinicians assess patient's response to the medication; results are reported and documented

Note: Information presented in red italicized text highlights the processes involved in selection and administration—key points in the process where users interact with products.

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