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Guidance Document for Industry - Review of Drug Brand Names

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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.

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Forward

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

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

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

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

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1 Introduction

1.1 Policy Objective

To provide market authorization holders direction on the process to be followed and information to be submitted to Health Canada regarding the potential for a proposed name to be misleading or confused with another product authorized for use in Canada with the aim of preventing medication errors.

1.2 Policy Statements

- Health Canada has the regulatory authority to consider brand names when making a decision on whether or not to grant a Notice of Compliance (NOC) or Drug Identification Number (DIN) to a sponsor.
- It is the responsibility of the sponsor to provide Health Canada with information to support the safety of a proposed brand name.
- Safety concerns are inclusive of issues that may arise due to lack of efficacy, i.e., the consequences of not receiving the intended drug to possible serious reactions, including death, resulting from receiving a product that was not intended for use.
- Health Canada will review the evidence submitted by the sponsor and may reject a brand name if in its judgement, the proposed name is misleading or has the potential to result in safety concerns if confused with the name (brand or non-proprietary name) of another product authorized for use in Canada.
- Safety issues may still arise once a product is marketed and used by healthcare professionals, patients and consumers on a day-to-day basis in an uncontrolled environment (as opposed to a controlled clinical trial environment). If a potential health risk is identified, Health Canada will address the issue and work in collaboration with a sponsor to develop mitigation strategies. Sponsors may be asked to change a name as a last resort if other risk mitigation strategies are not deemed sustainable.

1.3 Background

Medication incidents occur for a variety of reasons including confusion between health products with similar names. These similarities sometimes cause healthcare professionals and patients to confuse one health product name for another. Confusion can occur at any stage of the drug use process in inpatient, outpatient, and self-care settings. Depending on when they occur, they can cause prescribing errors, transcription errors, dispensing errors, administration errors and self-selection errors. The end result of a name confusion error is that the patient gets the wrong product. Wrong product errors harm patients by depriving them of the benefit of the correct treatment and by subjecting them, unknowingly, to the risks and adverse effects of the mistakenly selected health product. Such errors can and do cause serious harm, up to and including death.

Regulatory Authority

The *Food and Drug Regulations* require that a product name and an assessment of the brand name be provided in a drug submission as part of the information required to evaluate the safety and effectiveness of the product. The assessment is to determine that the names of drugs will not be confusable with one another. If confusion with the proposed brand name is considered likely and could result in safety concerns, then the Health Products and Food Branch (HPFB) can refuse to issue an NOC (for new drugs only) or a Drug Identification Number (for new drugs and existing drugs) as per C.01.014 and C.08.004 of the *Food and Drug Regulations*.

The *Food and Drug Regulations* also provide authority to the regulator to address safety issues when identified post-market. If a potential health risk with a brand name is identified, Health Canada will work with the manufacturer to

address the issue. Sponsors may be asked to change the brand name of the product as a last resort if long term mitigation strategies are not considered sustainable. Health Canada may invoke C.08.006 or C.01.013 of the *Food and Drug Regulations* in situations where the sponsor is not willing to comply.

Pre-Authorization Authorities under the *Food and Drug Regulations*:

Health Canada has the regulatory authority to consider brand names when making a decision on whether or not to grant a Notice of Compliance and issue a Drug Identification Number to a sponsor. As per the *Food and Drug Regulations*:

- C.01.014.1(2) sets out what must be included in an application for a DIN which includes:
 - (f) the brand name under which the drug is to be sold
 - (o) in the case of a drug for human use, an assessment as to whether there is a likelihood that the drug will be mistaken for any of the following products due to a resemblance between the brand name that is proposed to be used in respect of the drug and the brand name, common name or proper name of any of those products:
 - (i) a drug in respect of which a drug identification number has been assigned,
 - (ii) a radiopharmaceutical, as defined in section C.03.201, in respect of which a notice of compliance has been issued under section C.08.004 or C.08.004.01 and
 - (iii) a kit, as defined in section C.03.205, in respect of which a notice of compliance has been issued under section C.08.004 or C.08.004.01.
- C.01.014 to C.01.014.3 provides the requisite legal authority to refuse to issue a DIN to include situations where a specific drug has a similar name to another, thus placing users at risk.
- C.08.002(2), requires a submission contain sufficient information and material to enable the Minister to assess the safety and effectiveness of a new drug, including the following relevant subsection:
 - (b) a statement of the brand name of the new drug or the identifying name or code proposed for the new drug sold;
 - (o) in the case of a new drug for human use, an assessment as to whether there is a likelihood that the new drug will be mistaken for any of the following products due to a resemblance between the brand name that is proposed to be used in respect of the new drug and the brand name, common name or proper name of any of those products:
 - (i) a drug in respect of which a drug identification number has been assigned,
 - (ii) a radiopharmaceutical, as defined in section C.03.201, in respect of which a notice of compliance has been issued under section C.08.004 or C.08.004.01 and
 - (iii) a kit, as defined in section C.03.205, in respect of which a notice of compliance has been issued under section C.08.004 or C.08.004.01.
- C.08.002(3) permits the Minister to further require additional information or material that is considered necessary to assess the safety and effectiveness of the new drug.

Where Health Canada is not satisfied in its queries and it is evident that a potential safety risk exists with the proposed brand name, Health Canada is entitled to refuse to issue a NOC/DIN in accordance with subsections C.01.014.2 and C.08.004 of the *Food and Drug Regulations*.

Post-Authorization Authorities under the *Food and Drug Regulations*:

The regulator may invoke the following two sections of the *Food and Drug Regulations* if a potential health risk is identified post-market:

- Suspension of NOC: C.08.006(2)(f) provides the authority to suspend (for a definite or indefinite period) the NOC based on new information obtained after the issuance of the NOC that the brand name of a drug is or has been shown to be misleading. Under the section, the suspension follows the failure of the manufacturer to correct this problem following written notice.
- Stop Sale: C.01.013 provides the authority to direct a manufacturer to stop sale of a drug when it fails to submit evidence sufficient to establish the safety of a drug by a specific date.

Policy History

In January 2006, Health Canada's *Guidance for Industry - Drug Name Review: Look-alike Sound-alike (LA/SA) Health Product Names* became effective.¹ The guidance stated Health Canada's expectations and sought to generate consistency in the information submitted by sponsors regarding the impact of a proposed name on the safe use of a health product. However, internal analysis of LASA-related submissions since the release of the 2006 guidance has revealed significant variation in the amount, type, and quality of the evidence submitted by sponsors. This analysis, along with requests from industry for greater direction and continuing public concern about medication incidents due to LASA names, suggested that there was an opportunity to improve public health by revisiting the 2006 guidance on LASA names.

This guidance is intended to provide Health Canada with objective information in a standardized format. The availability of more and better evidence about the likelihood of confusion will allow Health Canada to make more informed decisions about the acceptability of a name.

1.4 Scope and Application

General

This guidance applies to the following drugs for human use (innovator and generic) in which a brand (proprietary) name is proposed:

- Pharmaceutical prescription drugs
- Schedule D products (e.g., Biologics)
- Schedule C products (e.g., Radiopharmaceuticals, kits)
- Drugs that are sold to the general public with the intervention of a healthcare professional, usually a pharmacist (e.g., nitroglycerin, insulin, injectable epinephrine for anti-allergic purposes)
- Drugs that are sold directly to healthcare professionals and are intended for professional use. (e.g., anaesthetics)

A generic drug where the manufacturer's name or an abbreviation of the manufacturer's name is combined with the proper/common (non-proprietary) name is considered a brand name (e.g., Canada-Furosemide Tablets or Can-

Furosemide Tablets where Canada is the manufacturer's name, Can is the abbreviation of the manufacturer's name and the product is furosemide).

The addition of a modifier² to a non-proprietary name is also considered a brand name.

This guidance does not apply to:

- Disinfectants;
- A proposed proper/common (non-proprietary) name of the medicinal (active) ingredient and the drug product in final dosage form as defined by section C.01.001 of the *Food and Drug Regulations*. Some examples include: Furosemide Tablets, Sodium Chloride Injection, Benzoyl Peroxide; and
- Non-prescription (over-the-counter) products and natural health products

A separate brand name assessment framework will be developed for non-prescription (over-the-counter) products and natural health products.

Review of Brand (Proprietary) Names

The purpose of a brand name review is to assess a proposed name to determine if it could be misleading or confused with another authorized product for use in Canada with the aim of preventing medication errors. All brand names must undergo an initial brand name review as outlined in Section 2.2. to assess for naming practices that could render proposed name misleading. Some, however not all brand names, will require a LASA brand name assessment (see section below on LASA brand name assessment-inclusions and exclusions). A LASA brand name assessment is used to assess the likelihood of confusion between a proposed name and other product names already authorised for use in Canada. A LASA brand name assessment should not be initiated prior to evaluating the proposed brand name against the criteria in section 2.2 as there may be circumstances that will prevent Health Canada from starting further review.

LASA Brand Name Assessments

Not all brand names require a LASA Brand name assessment. The information outlined below provides a list of inclusions and exclusions.

Inclusions:

A LASA brand name assessment is required for (S)(A)NDS submission types and DIN Application types wherein a brand name is being proposed or where a change to an existing brand name is being proposed (as per sections C.08.002(2)(o), C.08.002.1(2)(a), C.08.003(3.1)(b) and C.01.014.1(2)(o) of the *Food and Drug Regulations*). This includes:

- New Drug Submission (NDS)*;
- Supplement to a New Drug Submission (SNDS)*;
- Abbreviated New Drug Submission (ANDS)*;
- Supplement to an Abbreviated New Drug Submission (SANDS)*; and
- Applications for Drug Identification Numbers - DINA and DINB (including labelling only).

*Includes priority reviews, NOC with conditions and labelling only.

Exclusions:

Brand names that contain the proper or common name(s) in final dosage form in combination with a modifier, the manufacturer name or an acceptable abbreviation of the manufacturer name. Some examples include: Canada-Furosemide Tablets, Can-Furosemide Tablets (where Canada is the manufacturer and the product is furosemide). These will not require a LASA brand name assessment.

1.5 Process

General

A brand (proprietary) name is not essential to obtain a NOC/DIN for a drug submission. An NOC/DIN can be issued under the drug's common/proper name. However, in this case, a sponsor may not sell the product under a name other than the common/proper name without filing a supplemental submission and obtaining an NOC or DIN for a different product name. If a LASA brand name assessment is required at time of submission however is not provided, the *sponsor* will be notified. In the case of a labelling only submission, the brand name assessment will be requested through a Screening Deficiency Notice. Failure to provide a LASA brand name assessment will result in the brand name being deemed unacceptable and Health Canada will move forward with the use of the proper/common name (see below for further details).

For submissions of 180 days or greater that require a LASA brand name assessment, a maximum of 2 brand names will be reviewed. Sponsors must identify which brand name has priority for review. Health Canada will review one brand name at a time. The alternate name will not be reviewed or considered for confusion with other proposed or marketed products authorised for use in Canada until agreement has been reached between Health Canada and the sponsor that the first brand name is no longer under review or further consideration.

If a brand name is deemed unacceptable, sponsors will be notified and:

- The sponsor may confirm to Health Canada to move forward with the review of the alternate name and LASA brand name assessment; or
- The sponsor may indicate to Health Canada that they do not want to have the alternate name reviewed and submit a new brand name and LASA brand name assessment; or
- Health Canada will move forward with the use of the proper/common name and the drug submission will be issued a NOC or DIN if the proposed brand name is the only outstanding issue with the drug submission.

For submissions of less than 180 days that require a LASA brand name assessment (e.g., labelling only), only one name will be reviewed within the timelines and associated fees.

If a sponsor does not wish to move forward with the use of the proper/common name and all brand names are deemed unacceptable, a Notice of Non-Compliance (NON) will be issued (C.01.014.2 and C.08.004 of the *Food and Drug Regulations*). For submissions of less than 180 days, since only one name will be reviewed, the sponsor's response to a NON may include information to address the concerns but proposals for a different new name should be filed in a new submission. Sponsors may formally reconsider the decision if it results in a Withdrawal Notice according to Health Canada's "Guidance for Industry: Reconsideration of Final Decisions Issued for Human Drug Submissions"³.

For any product and at any time, Health Canada reserves the right to request information or material, or define conditions not specifically described in this document in order to allow the Department to adequately review the safety, efficacy or quality of a drug (C.08.002 of the *Food and Drug Regulations*) to protect the public. Requests for information may include raw data generated during the name assessment process. Health Canada is committed to ensuring that such requests are justifiable and that decisions are clearly documented.

Health Canada may reject a name if it considers, based on review of the information provided, that the name is likely to cause confusion with other health products, or is misleading with respect to the therapeutic effectiveness, composition or the safety of the product.

Review Timelines

Health Canada will review a sponsor's brand name assessment as part of the drug submission within the performance standard outlined in Appendix 3 of the Management of Drug Submissions Guidance Document depending on the applicable submission type.⁴ Associated fees are provided in the "*Guidance Document: Fees for the Review of Drug Submissions and Applications*"⁵.

For submission types that involve a review target of 180 days or longer, Health Canada will complete an initial review of the name within the first 90 days of the submission being accepted for review. A second but abbreviated review will be conducted 30 days prior to issuance of NOC/DIN to confirm no other names have been approved recently with a potentially confusing name.

If the initial brand name is found to be unacceptable, a new brand name and assessment must be submitted within the time requested by Health Canada and at least 90 days prior to the review target date. If not submitted, the submission will be given an NOC/DIN for the proper/common name. A new submission to propose a brand name will be subject to all associated costs and timelines.

International Submissions

Some proposed brand names have undergone a global development and testing process with the goal of identifying a global brand name. This testing may or may not have involved Canadian respondents and given consideration to the use of the product in Canada.

If a LASA brand name assessment has been completed in another jurisdiction, there may be a need for additional assessment to reflect the Canadian context. The first step in determining the relevance of information to the Canadian context is to confirm through a Drug Product Database (DPD) and Licensed Natural Health Product Database (LNHPD) search that the LASA name candidates (i.e. the existing brand names that could be confused with the proposed brand name) are identical to those authorised for use in Canada. These LASA name candidates will have been generated via database searches, simulations and FMEA type processes. A difference in indication or other non-name attributes may render the name more or less likely to be confused in Canada and should be factored into the assessment.

It is also necessary to give consideration to the process maps (as identified in Section 2.3.2 Simulate) developed for the product. If the product will be used in much to the same way, the outcome of the simulations will be of relevance to making a decision about the acceptability of a name in Canada.

If the process map is similar, the name candidates are identical and a risk assessment process was completed, final consideration should be given to any issues that may arise due to the bilingual nature of the Canadian healthcare environment.

If required, Health Canada may request additional information to assess the safety of the proposed name for the Canadian market.

Administrative Drug Submissions

Any submission that requires LASA brand name assessment to support a name change for the drug product is not considered administrative and should be submitted for processing as a Labelling Only submission.

Post-Market Safety Issues

Safety issues may still arise once a product is marketed and used by healthcare professionals, patients and consumers on a day-to-day basis in an uncontrolled environment (as opposed to a controlled clinical trial environment). If a potential health risk with a brand name is identified, Health Canada will work with the sponsor to address the issue. Sponsors may be asked to change the brand name of the product as a last resort if long term mitigation strategies are not considered sustainable. Health Canada may invoke C.08.006 or C.01.013 of the *Food and Drug Regulations* in situations where the sponsor is not willing to comply.

All safety issues will be treated on a case-by-case basis. In situations where more than one manufacturer is implicated (e.g., look-alike sound-alike health product names), the manufacturer with the latest issued NOC will be contacted.

2 Guidance for Implementation

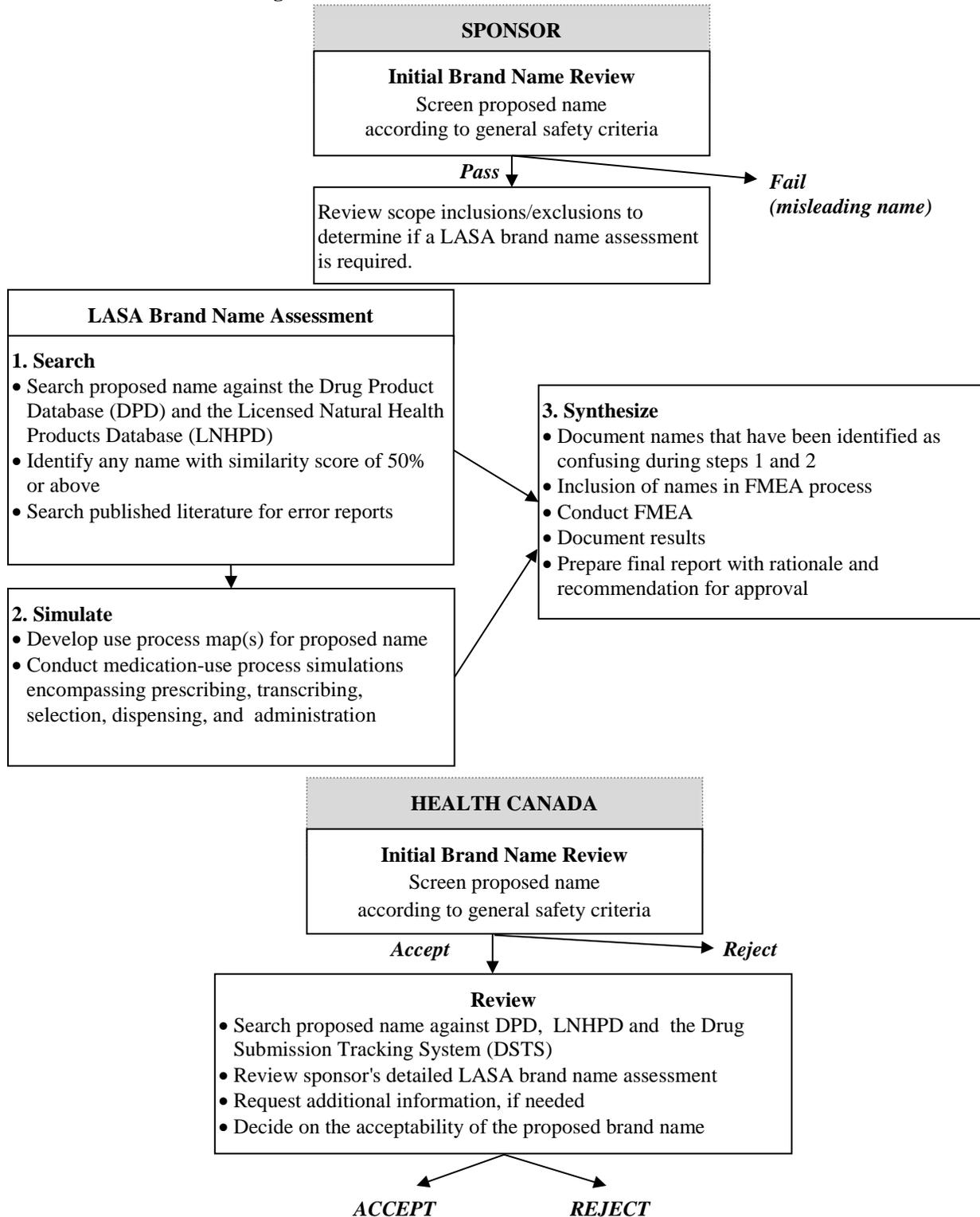
2.1 Brand Name Assessment Process

Assessment of proposed brand names is intended to determine if the name is misleading or could be confused with an existing product authorised for use in Canada (sections C.08.002(2)(o), C.08.002.1(2)(a), C.08.003(3.1)(b) and C.01.014.1(2)(o) of the *Food and Drug Regulations*).

Sponsors will be responsible for carrying out the initial brand name review and LASA testing procedures (where applicable) outlined in this guidance to demonstrate that their submitted brand name is not likely to be misleading or cause confusion with other health products that are authorised for use in Canada. Health Canada will review the information submitted and make the decision to approve or reject the proposed brand name.

The diagram below, Figure 1, outlines the process to be followed in completing a brand name assessment.

Figure 1: Brand Name Assessment and Review Process



2.2 Initial Brand Name Review

All brand names must undergo an initial brand name review. Sponsors should review each proposed brand name using the criteria outlined below. These criteria address naming practices that Health Canada view as misleading (per Section 9 of the *Food and Drugs Act*; A.01.017 and C.08.006 of the *Food and Drug Regulations*).

A proposed brand name must pass the initial brand name review to be considered for approval. An affirmative response to any of the questions one through seven will result in a proposed name failing the initial brand name review. In these circumstances, Health Canada will contact the Sponsor to request an alternate brand name, accompanied by a LASA brand name assessment, if applicable.

Initial Brand Name Review Criteria

1. Does the name/modifier suggest/imply an unsubstantiated unique effectiveness/composition, superiority claims, exaggerated product efficacy, broadening product indication or minimizing the risk of the product (e.g., making superiority claims such as ‘CureAll’)?
2. Does the name/modifier include or imply an ingredient that is not included in the drug product?
3. Is the name identical to an authorized product in Canada containing a different medicinal ingredient(s) (e.g., ‘Podium’ contains the medicinal ingredients ‘XY’ and a sponsor proposes the identical name ‘Podium’ for medicinal ingredient ‘Z’)?
4. Does the proposed name contain a letter sequence/stem that is in the same position designated by USAN (U.S. Adopted Name) or INN (International Nonproprietary Name) for the same or different pharmacological/chemical trait?^{6,7,8}
5. Does the proposed brand name contain or suggest an exclusive composition of only one ingredient in a multi-ingredient product?
6. Does the name suggest an unsupported route of administration or dosage form?
7. Does the name conflict with Schedule A of the *Food and Drugs Act* (e.g., DiabeticCare™ Acetaminophen Tablets)?

Below is a list of additional factors that are given consideration by Health Canada when making a decision about the acceptability of a proposed brand name. Although these factors will not lead to an automatic rejection of the proposed name, they will require the sponsor to provide a rationale supporting why this approach can be used without the risk of being misleading or resulting in confusion.

- Was the same/similar name used previously for a product that is no longer available on the market (i.e., discontinued)?
- Does the name contain a confusable abbreviation?⁹ (e.g. QD may be read or interpreted as QID, OD may be interpreted as either *Oculus Dexter* [Latin, meaning ‘right eye’] or Once Daily) (See Appendix 2 for further information on abbreviations.)
- Does the modifier contain a single letter or number?¹⁰ (See Appendix 2 for further information on the use of modifiers.)
- Might the modifier hinder the health professional/consumer in selecting the appropriate medication? (See Appendix 2 for further information on the use of modifiers.)
- Does the brand name or part of the brand name represent or imply a medical and/or scientific term or acronym?
- Does the proposed name contain a letter sequence/stem that is in a different position designated by USAN or INN for the same or different pharmacological/chemical trait^{11,12,13}?

- Is the proper/common name abbreviated or truncated?
- Are you aware if the name has been approved in another country for a product with a different medicinal ingredient?

2.3 Testing of Proposed Brand Names for Look-alike Sound-alike Attributes

For a proposed name that has passed the initial review and requires a LASA brand name assessment, a multistep procedure will be used by sponsors to assess the likelihood of confusion between the proposed name and product names that are authorised for use in Canada. The multistep process will involve database searches, medication-use simulations and critical synthesis of findings i.e. *Search, Simulate, Synthesize*.

2.3.1 Search

This step involves systematic searching of relevant drug name and medication error databases. The information retrieved during this step provides an initial list of drug names that merit further scrutiny during the final step, *Synthesize*.

A number of commercial search engines exist for assessing the orthographic and phonetic similarity of brand names. Sponsors are to search the Drug Product Database (DPD)¹⁴ and the Licensed Natural Health Products Database (LNHPD) by submitting the proposed name as a query to a health product name search engine.¹⁵ The search engine will return a list of health product names, ranked in descending order of similarity to the query name, where similarity is measured by an objective computer algorithm.¹⁶ Any name with a combined orthographic and phonetic score greater than or equal to 50% similarity is to be included in the search results submitted to Health Canada.

If the proposed brand name is already marketed in another country, sponsors are to search the published literature, as well as medication error databases, and submit the results of those searches to Health Canada. The goal is to identify any previously reported name confusion errors. This information should be gathered via a search of several sources, which can include internal sponsor databases, ISMP/ISMP Canada published reports and databases, MedMarx database, PubMed, and the International Pharmaceutical Abstracts.

Sponsors are to assess the information generated by the drug name search engine during the third and final step, *Synthesize*. All raw data from the database search must be submitted to Health Canada with the date of completion clearly identified.

Health Canada will conduct a search of the Drug Submission Tracking System (DSTS) to identify any brand names in the submission review process that could be candidates for confusion with the proposed name. Health Canada, through its searches of the DPD and LNHPD using the Phonetic and Orthographic Computer Analysis (POCA) application, will verify that all names of concern with a combined orthographic and phonetic similarity score equal to or greater than 50% have been included for assessment during the *Synthesize* step.

2.3.2 Simulate

The purpose of simulation experiments is to assess the confusability of a proposed name by inserting it into a variety of prescribing, transcribing, dispensing and administration scenarios and documenting the resulting failures (i.e., the number and type of errors that occur).

2.3.2.1 Process Maps

In order to create a context for planning and evaluating the simulations, sponsors are to prepare and submit a process map(s) that outline where and how the proposed brand named drug will be used, based on its indications and who in the medication use system will come into contact with the product. Process maps are to be prepared according to the most common use settings and circumstances as well as the highest potential risk situations (where applicable).

The medication use system involves many processes—from the point of a product being considered for addition and use in a practitioner's armamentarium to final administration and subsequent monitoring of its effects. Medication reconciliation is also an aspect of the medication use system that should be considered.

Prescribing Where a product is a prescription drug, prescribing could be performed by a medical doctor, dentist, podiatrist, nurse practitioner, or other healthcare professional with prescribing privileges.

Transcription occurs when a product is ordered verbally and the order is written down by someone else, such as a nurse or a pharmacist, or perhaps a ward clerk or a technician in a hospital setting. It can also occur when records are copied and during medication reconciliation.

Dispensing can be performed by a pharmacist in a community pharmacy or hospital, by an assistant or nurse, or a doctor in his/her office.

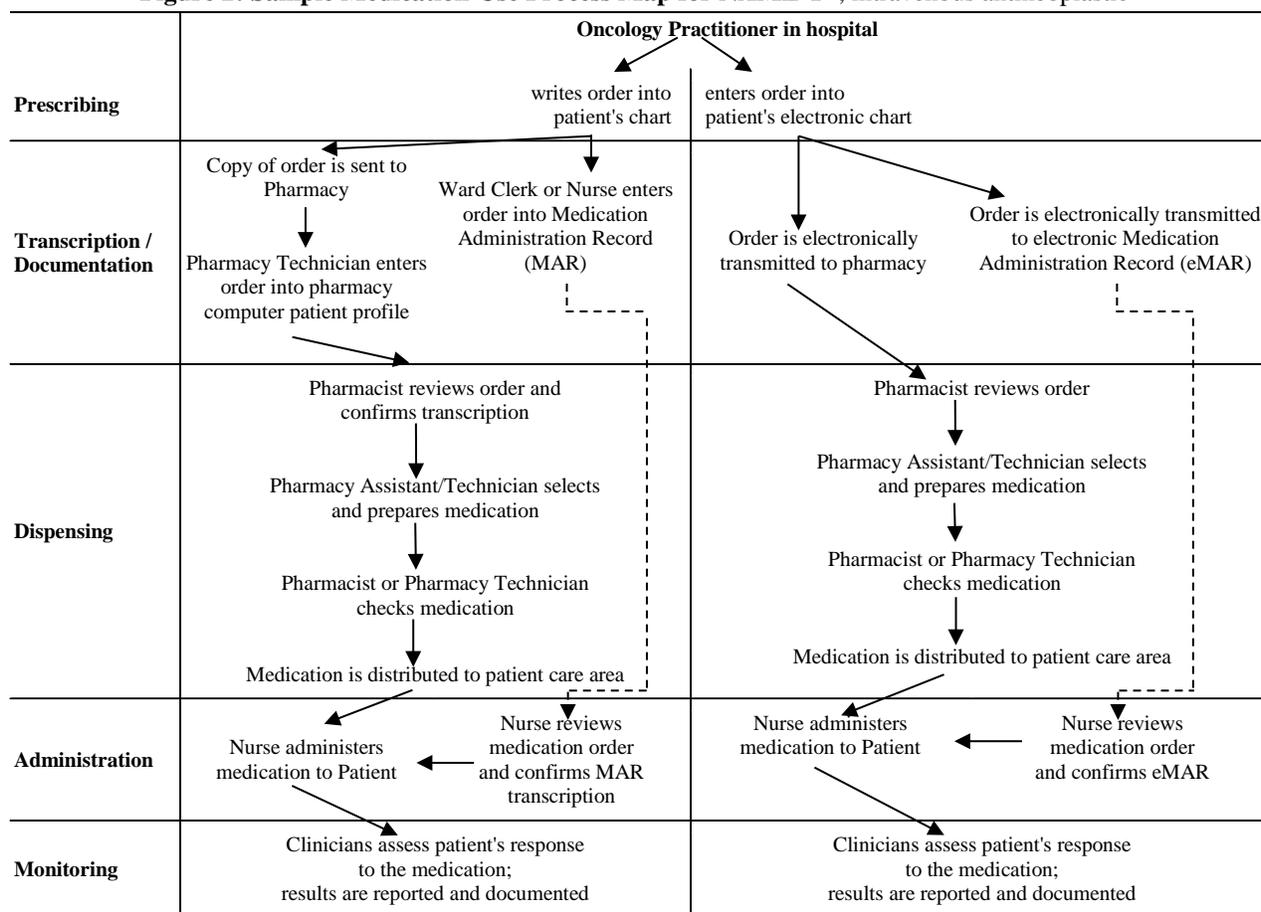
Administration. Doctors, nurses and other healthcare professionals may be involved in administering a product.

Monitoring takes place after a product is administered and follow-up occurs.

Where applicable, patients should be identified in the process maps.

The human-computer interface occurs in many areas of the medication-use system—in healthcare facilities, community pharmacies and in doctors' offices. The process map needs to include, where applicable, the use of computers and electronic information. An example of a medication-use process map is presented in Figure 2, below. Additional examples can be found in Appendix 3.

Figure 2: Sample Medication-Use Process Map for NAME Y[®], intravenous antineoplastic



2.3.2.2 Medication-Use Process Simulations

Given the nature of how Schedule C products (e.g., radiopharmaceuticals, kits) are managed and utilized, simulation exercises will not be required.

The primary purpose of the name simulation studies is to gather data about possible risks of confusion involving a proposed brand name in a simulated clinical scenario. Practising healthcare professionals, ancillary staff and patients where applicable e.g. outpatient settings participate in the simulations with the goal of identifying the potential hazards, errors, and failure modes related to the use of the name. The information gathered during the name simulation studies is collated and assessed along with the names identified during the search of reference databases in the last step of the name review process, Synthesize.

Using the medication-use process map developed in Section 2.3.2.1, the proposed name is communicated and processed in much the same way as it would be in real-world circumstances. The number of different drug use scenarios will vary depending upon the type of product being tested. For example, an injectable drug used only in the operating room setting would have far fewer scenarios than an oral prescription drug.

Although the submitted process map(s) are to be comprehensive, simulations do not need to involve all mapped pathways. Key pathways are to be identified according to the most common use settings and

circumstances as well as the highest potential risk situations. It is important for the simulations to capture the main modes of communication—spoken, handwritten, faxed, electronically submitted—and to involve key members of the healthcare team (e.g., physician, ward clerk, nurse, receptionist, pharmacist, technician) as well as the patient when appropriate.

Participants should be representatives of both French and English speaking populations. Statistics indicate that the francophone represents approximately 21% of the Canadian population. It is therefore recommended that French speaking Canadians account for 20-25% of participants represented in the simulation exercises for the testing of proposed brand names.¹⁷

The number of scenarios tested will depend on the submitted medication-use process map(s) and the identification of key usage pathways for the product. Sponsors will be required to submit the findings from at least 5 medication-use process simulations. These can be single replications of at least 5 scenarios, or multiple replications of single scenarios. The scenarios can be played out by multiple individuals, but each individual must only ‘process’ the proposed name once to avoid familiarity and learning. A minimum of 100 Canadian healthcare professionals must participate in the medication-use simulations unless a strong case can be made for a smaller number due to the specialised nature of the product and its intended users.

When the simulations are completed, the participants are debriefed according to a structured protocol and are required to answer a standard set of questions about the proposed brand name. (See Appendix 4 for more details on medication-use process simulation.)

2.3.3 Synthesize

The database search results together with the simulations generate complementary lines of evidence necessary to help make a decision about the likelihood of confusion with the proposed name. In the final step, sponsors are to complete a failure mode and effects analysis (FMEA) and synthesize the information gathered throughout the name testing process.

In preparation for the FMEA, sponsors are to prepare a table that lists all the drug names that were identified across the search and the simulation tests that could be confused with the proposed brand name. After having listed the names, the sponsor will provide a rationale as to why the names will be included or excluded from the FMEA, e.g., the name is of a disinfectant or veterinary product.

2.3.3.1 Failure Mode and Effects Analysis

Sponsors are to put their proposed product name through an FMEA process and demonstrate that the proposed name has no significant failure modes, or at least none so significant as to prevent the name from being approved.

FMEA is a proactive technique to identify process and product problems before they occur. It involves the analysis of a product or process by domain experts of practicing physicians, pharmacists, nurses and other health professionals. The FMEA team includes active practitioners in the field of use for the product whom handle/prescribe the drug (orders) in the various specialty areas in distinct practice settings and circumstances. These ‘experts’ seek to identify all potential things that can go wrong with a process or product (i.e., its failure modes).

In the context of this guidance, the FMEA panel members will use the submitted medication-use process map(s), which plot(s) the drug's passage through the healthcare system—from procurement and distribution activities to ordering/prescribing, selection, manipulation (if required), dispensing, administration, patient monitoring, medication reconciliation etc. Furthermore, all the drug names identified as potentially confusable in the Search and Simulate steps (excluding those that were discarded with the rationale), and those generated by the panel members are to be considered in the FMEA.

The FMEA is to include comparisons of overlapping characteristics of the confusable drug names with the profile of the proposed product. The following product profile criteria, or non-name attributes, are to be considered in completing the analysis: marketing status (Rx or non-prescription), therapeutic category, medicinal ingredient, indication(s), clinical setting for dispensing or self-selection, strength, dosage form, route of administration, proposed dose, dosing interval/frequency and storage (e.g., refrigerated or room temperature). Additional examples of attributes to take into consideration in determining the degree of similarity are provided in Appendix 5. Each of the transaction points is discussed by the panel of experts to identify failure modes. Each of the failure modes is then discussed to determine how easily it might be avoided and the severity of the potential consequences should the failure mode occur.

The analysis completed by the FMEA panel members is to also address and document responses to the following questions:

- 1) Are any of the drugs that could be confused with the proposed brand name:
 - a) a high alert drug or a drug with a narrow therapeutic index¹⁸
 - b) a pharmacological opposite
 - c) a product with significant contraindications or warnings and precautions,
 - d) a product with known drug interactions or allergies
 - e) a product with a high prescribing frequency

- 2) Omitting the drug
 - a) What are the consequences of omitting the intended drug?
 - b) What would be the consequences of omitting the intended drug in special patient populations, e.g., paediatrics, patients who are pregnant, elderly, nursing, or have compromised liver or kidney function?
 - c) How long could a patient go without the intended treatment before being adversely affected?

- 3) Wrong drug therapy
 - a) What are the consequences of being exposed to the wrong drug (i.e., all the confusable drug names identified in Search and Simulate steps and by the FMEA panel)?
 - b) What number of doses would need to be administered to cause harm?
 - c) What would be the consequences of receiving the wrong drug in special patient populations, e.g., paediatrics, patients who are pregnant, elderly, nursing, or have compromised liver or kidney function?

- 4) Combined drug therapy
 - a) What are the consequences of combined drug therapy?
 - b) Is there a potential to exacerbate adverse reactions due to differing drug profiles?

A summary report is to be prepared which highlights the major identified vulnerabilities of the name (if any), based on the panel's input. An example of an FMEA approach is shown in Appendix 6.

2.3.3.2 Synthesize

A report summarizing all the findings from the LASA brand name assessment, i.e., the Search and Simulate steps and the FMEA, must be submitted to Health Canada. Furthermore, a cumulated list of all the names generated from every component of the assessment process including those that were eliminated with rationale, i.e., the Search and Simulate steps and the FMEA, must be submitted. A final rationale for the approval of the proposed name for marketing in Canada is to be presented. Where certain findings are excluded, an explanation must be provided as to why they do not present an obstacle to approval.

2.4 Decide

This guidance is intended to provide Health Canada with objective information in a consistent format. The intent is that the availability of better evidence about potential confusions will allow Health Canada to make more informed decisions, thereby protecting the public from the consequences of medication errors due a drug's brand name.

The final phase involves Health Canada reviewing the information submitted by sponsors and making a decision about the acceptability of the proposed name. In addition to reviewing the information submitted by sponsors, Health Canada will complete a search of Health Canada's Drug Submission Tracking System to identify any names in the submission process that give rise to concern due to the potential for confusion.

As a regulator, Health Canada reserves the right to request information or material (including raw data when necessary), or define conditions not specifically described in this document, in order to allow the Department to adequately assess the safety, efficacy or quality of a drug (C.08.002 and C.01.014 of the *Food and Drug Regulations*). Health Canada is committed to ensuring that such requests are justifiable and that decisions are clearly documented.

Health Canada may reject a name if it considers, based on the information provided or in its own review, that the name is likely to cause confusion with other health products, or is misleading with respect to the therapeutic effectiveness, composition or the safety of the product.

Safety issues may still arise once a product is marketed and used by healthcare professionals, patients and consumers on a day-to-day basis in an uncontrolled environment (as opposed to a controlled clinical trial environment). If a potential health risk with a brand name is identified, Health Canada will work with the sponsor to address the issue. Sponsors may be asked to change the brand name of the product if long term mitigation strategies are not considered sustainable. Health Canada may invoke C.08.006 or C.01.013 of the *Food and Drug Regulations* in situations where the sponsor is not willing to comply.

Appendix 1 - Definitions

Authorized Product: A product that has been approved by Health Canada.

Brand Name (or proprietary drug name): C.01.001.(1) of the *Food and Drug Regulations* states that a “brand name” means, with reference to a drug, the name, whether or not including the name of any manufacturer, corporation, partnership or individual, in English or French, (a) that is assigned to the drug by its manufacturer, (b) under which the drug is sold or advertised, and (c) that is used to distinguish the drug.

Sponsors must declare the entire product name as it will appear on the final labelling in box 8 of the Drug Submission Application Form (Health Canada3011).

Failure Mode and Effects Analysis (FMEA): A team-based systematic and proactive approach for identifying the ways that a process or design can fail, why it might fail, the effects of that failure and how it can be made safer. FMEA focuses on how and when a system will fail, not *if* it will fail. (ISMP Canada)

Generic Name: The generic (also known as non-proprietary and established name) describes the drug substance. International Non-proprietary Names are created to identify generic names as unique, universally applicable and accepted names. A generic name is the proper name of an ingredient, or the common name if the ingredient has no proper name.

High-Alert Medications: A drug known to present serious risk of harm due to its pharmacological properties (e.g., paralytic drugs, opioid analgesics, concentrated electrolytes). These medications have a high risk of causing injury when they are misused.¹⁹ Most medications have a moderate margin of safety, yet a small number of drugs have a high risk of causing injury when they are misused. These are called ‘high-alert medications’ to draw attention to this characteristic, and so all involved in their use will handle them with the care and respect they require. Errors may or may not be more common with the use of these drugs compared to others. However, the consequences of the errors are more devastating and their use requires enhanced precautions. These medications often need to be packaged differently, stored differently, prescribed differently, dispensed differently and administered differently than most other medications.

Note: Definition adapted from the Institute for Safe Medication Practices (ISMP).

Immediate Container: C.01.001 of the *Food and Drug Regulations* states that an immediate container is *the receptacle that is in direct contact with a drug*.

International Nonproprietary Name (INN): The INN identifies a drug substance by a unique, universally applicable and accepted generic name. It is noted that chemicals that do not have a defined chemical composition or structure or that cannot adequately be described cannot be assigned INNs (i.e., mixtures of substances).^{7,8,20,21}

Label²² - Section 2 of the *Food and Drugs Act* states that the label *includes any legend, word or mark attached to, included in, belonging to, or accompanying any food, drug, cosmetic, device or package*.

Label (Inner) - A.01.010 of the *Food and Drug Regulations* states that the inner label is *the label on or affixed to an immediate container of a food or drug*.

Label (Outer) - A.01.010 of the *Food and Drug Regulations* states that the outer label is *the label on or affixed to the outside package of a drug*. For example, the label on a box containing a bottled drug.

Look-Alike Sound-Alike (LASA) Health Product Names: Health products that have a similar written name or similar phonetics to those of another health product.

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.²³ Similar Term: Medication Error.

Medication-Use System: The system that encompasses the drug's passage from procurement and distribution activities to the continuum of (1) prescribing by the clinician (or self-prescribing), followed by transcribing; (2) preparing and dispensing by the pharmacist; (3) administering by the provider or consumer (self-care); (4) monitoring for therapeutic and adverse effects (by healthcare professional, surrogate, or self); and medication reconciliation at transitions of care. Each of these steps includes critical control points at which decisions and actions can contribute to safety or errors.

Near Miss or Close Call: An event that could have resulted in unwanted consequences, but did not because either by chance or through timely intervention the event did not reach the patient. Similar Terms: Near Hit or Good Catch.

Non-Proprietary Name:

Chemical Name: The Chemical name of a drug which provides an unambiguous picture of a molecule so that a trained chemist can use it to draw its structure if required {i.e., 4-(4-(p-chlorophenyl)-4-hydroxypiperidone)-4'-fluorobutyrophenone is the chemical name for Haloperidol}.

Common Name: *C.01.001.(1) of the Food and Drug Regulations states that a 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 publication referred to in Schedule B to the Act.*

Proper Name: *C.01.001.(1) of the Food and Drug Regulations states that a "proper name" means, with reference to a drug, the name in English or French (i) assigned to the drug in section C.01.002, (ii) 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, (iii) specified in the Canadian licence in the case of drugs included in SCHEDULE C or SCHEDULE D to the Act, or (iv) assigned in any of the publications mentioned in SCHEDULE B to the Act in the case of drugs not included in subparagraphs (i), (ii) or (iii) of this paragraph.* For products with multiple ingredients, there is no proper name for the product but there is a proper name for each ingredient. Example of a proper name – Acetaminophen, Azithromycin Capsules

Package: In the context of this document, the term package *includes any thing in which any food, drug, cosmetic or device is wholly or partly contained, placed or packed, from Section 2 of the Food and Drugs Act.*

Note: The terms 'package' and 'packaging' are used synonymously for the purposes of this document, and mean package as defined here.

Product Characteristics: The physical characteristics of the product itself (i.e., dosage form, strength, medicinal ingredient) and environment in which the product is used, including but not limited to the established name, label,

labelling, container, facility, storage conditions, who prescribes and administers the product, patient population, and other conditions of use.

Proprietary drug name (or Brand Name): C.01.001.(1) of the *Food and Drug Regulations* states that a “brand name” means, with reference to a drug, the name, whether or not including the name of any manufacturer, corporation, partnership or individual, in English or French, (a) that is assigned to the drug by its manufacturer, (b) under which the drug is sold or advertised, and (c) that is used to distinguish the drug.

Trade Name: Section 2 of the *Trade-marks Act* states that a trade name is the name under which any business is carried on, whether or not it is the name of a corporation, a partnership or individual.

United States Adopted Name (USAN): USAN identifies nonproprietary names for drugs by establishing simple, logical nomenclature based on pharmacological and/or chemical relationship. The USAN committee develops the names, taking into account practical considerations, such as the existence of trademarks, international harmonization of drug nomenclature, the development of new classes of drugs, and the fact that the intended uses of substances for which names are being selected may change.⁶

Real World Safe Use: Term used to describe the use of a product by healthcare professionals, patients and consumers on a day-to-day basis in an uncontrolled environment (as opposed to a controlled clinical trial environment).

Trade Mark: Section 2 of the *Trade-marks Act* states that a trade-mark is (a) a mark that is used by a person for the purpose of distinguishing or so as to distinguish wares or services manufactured, sold, leased, hired or performed by him from those manufactured, sold leased, hired or performed by others, (b) a certification mark, (c) a distinguishing guise, or (d) a proposed trade mark.

Appendix 2 – Modifiers/Abbreviations

The use of modifiers/abbreviations in a name can create opportunities for error and misinterpretation. Health Canada will review proposed modifiers/abbreviations from the point of view of safety and confusability. Sponsors are to provide a rationale for the necessity of a modifier/abbreviation, its potential for safe use and any available studies that corroborate the intended meaning of the proposed modifier.

Acceptable modifiers/abbreviations should meet the following minimum criteria:

- Modifiers should reinforce in a clear manner existing information on the label and thus aid the health professional/consumer to select the appropriate medication.
- The modifier should provide useful and easily identifiable information to the health professional/consumer.
- The modifier should not be ambiguous or otherwise have the potential to be misinterpreted by health professionals/consumers and thus result in medication incidents. For example, abbreviations that indicate dosing schedules should be avoided. (QD may be read or interpreted as QID, OD may be interpreted as either *Oculus Dexter* [Latin, meaning ‘right eye’] or Once Daily).
- Generic versions should contain the same modifier to the brand name version or innovator product to distinguish the different indications or dosing considerations, where permissible with respect to copyright/trademark law.
- Consideration should be given to the potential risk or benefit to the patient in the case of using the modifier versus an alternate brand name.
- Consideration should be given to the consequences of the accidental omission of the modifier in the brand name during the medication use system from procurement and distribution activities to prescribing/ordering, selection, manipulation (if required) dispensing, administration and patient monitoring. For example, if there are identical strengths, a medication incident is more likely to occur.

Refer to the Institute for Safe Medication Practices²⁴ and the National Coordinating Council on Medication Error Reporting and Prevention²⁵ for a list of recognized high risk error-prone abbreviations that are to be avoided. As well, refer to Health Canada’s *Guidance for Industry – Labelling of Pharmaceutical Drugs for Human Use*.²⁶

Appendix 3 - Medication-Use Process Maps

Medication-use process maps outline where and how a drug will be used, based on its indications and who in the medication use system will potentially come into contact with it. Two examples for different products and contexts are provided. These diagrams identify the principal participants in the medication-use process, including non-healthcare or ancillary personnel and patients. The maps plot the passage of the drug through the healthcare system—from procurement and distribution activities to ordering/prescribing, selection, manipulation (if required), dispensing, administration, and patient monitoring.

Figure 3: Sample Medication-Use Process Map for NAME Y[®], intravenous antineoplastic drug

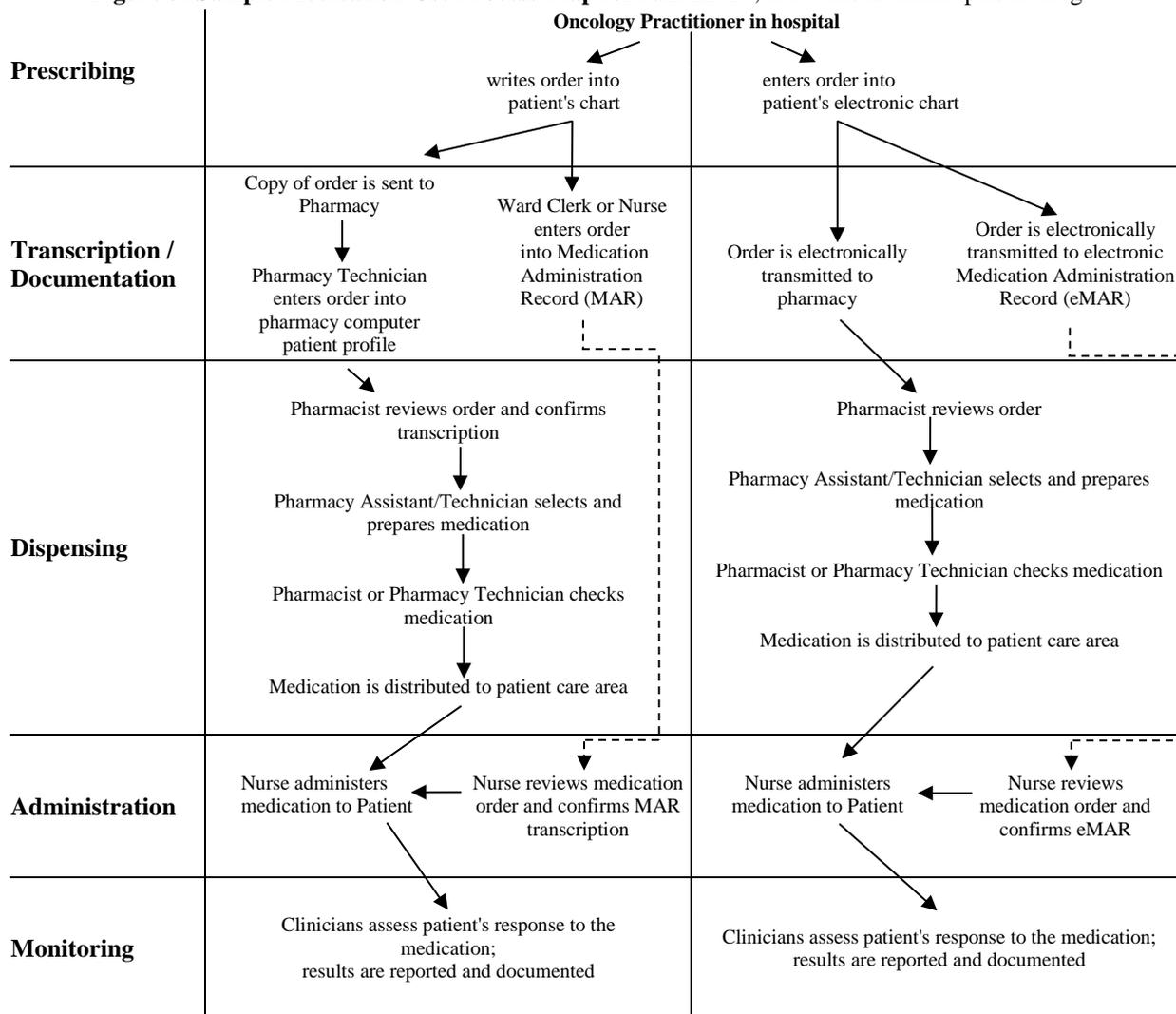
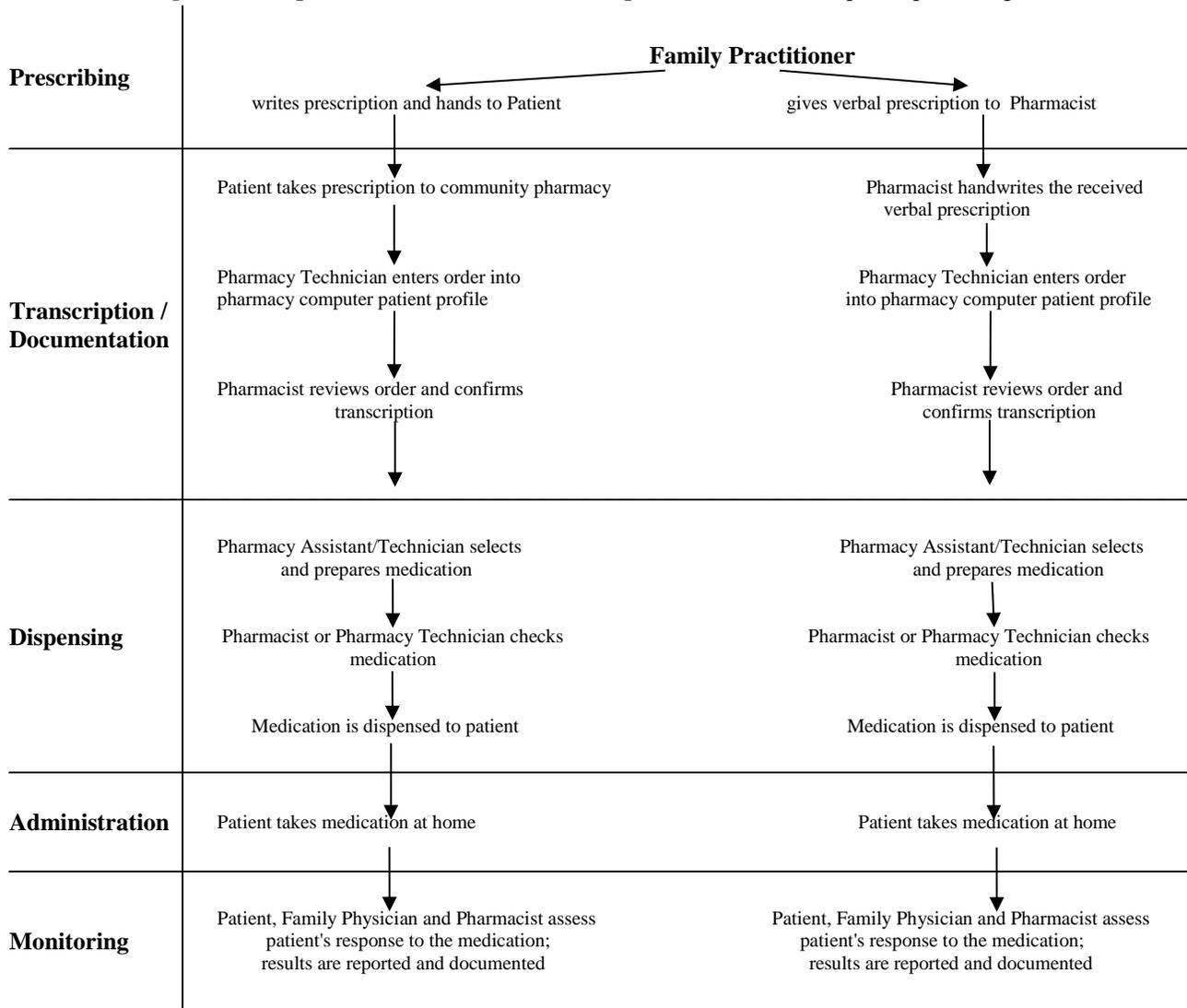


Figure 4: Sample Medication-Use Process Map for NAME Z[®], oral prescription drug



Appendix 4 - Medication-Use Process Simulation

In medication-use process simulation, proposed brand names for a single product are tested for their safety as they pass through various channels before being used by the patient, e.g., from the time a name is written by a prescriber then faxed to a pharmacy and finally delivered to a patient. Simulations should follow the medication-use process map developed for a particular product. The intention is not to determine whether a name is liked, but rather to do the following:

- 1) to evaluate its performance—its safety and clarity—when spoken, written, faxed and read; and
- 2) to identify how distinctive each name is compared to other drug product names and compared to other general products and terms.

One process example is shown below. (Note that for select drugs certain patient populations may have underlying conditions and may be taking other drugs that could contribute to confusion or add confounding elements.)

Table 1: Sample Medication-Use Process in the Primary Care Physician Setting

PATHWAYS (PCP Setting)	Written (handwritten & typed)	Spoken	Drug name under evaluation
PCP* recommends or prescribes product to Patient	PCP 1 to Patient 1 PCP 2 to Patient 2 (written to simulate in office process; prescription writing)	PCP 1 to Patient 3 PCP 2 to Patient 4 (simulates phone call if patient calls, and interpretation of the name when recommended or prescribed at visit)	<i>NAME</i>
PCP to PC* Nurse (include PCP to nurse for nonprescription drugs, in case nurse fields call from patient)	PCP 1 to PC Nurse 1 (written)	PCP 2 to PC Nurse 2	<i>NAME</i>
PCP to PC Secretary	PCP 2 to PCP Secretary 1 (written; simulates chart transcription)	PCP 1 to PC Secretary 2 (simulates transcription)	<i>NAME</i>
PCP to Pharmacist	PCP 1 to Pharmacist 1 (written)	PCP 1 to Pharmacist 2	<i>NAME</i>
PCP to Pharmacy Technician or Pharmacy Assistant	PCP 1 to Pharmacy Technician 1 (written, e.g., renewal of prescription or reading of PCP's note to patient)	PCP 1 to PA* 1 (e.g., renewal of prescription)	<i>NAME</i>
PC Nurse or Secretary to Patient	PC Nurse 3 to Patient 5	PC Secretary 3 to Patient 6	<i>NAME</i>

* Abbreviations: PCP = Primary care physician, PC = Primary care, PA = Pharmacy assistant

A minimum of 100 Canadian healthcare professionals must participate in the medication-use simulations unless a strong case can be made for a smaller number due to the specialised nature of the product and its intended users. Sponsors will be required to submit the findings from at least 5 medication-use process simulations. These can be single replications of at least 5 scenarios, or multiple replications of single scenarios.

Each participant processes only one transaction to avoid learning the drug name which would bias the results. However, one participant may leave a verbal and a written communication and each communication may be picked up by more than one participant. The number of scenarios can be greater than the number of participants. For example, one ‘prescriber’ can write and verbally transmit a number of drug names, which can be picked up for interpretation by any number of nurses, patients, other prescribers, secretaries, pharmacists, and pharmacy technicians, as long as each individual processes the name only once.

Healthcare professionals are provided with the test name. They then handwrite and fax the name or type and fax it to a predetermined fax line, or leave a voicemail on a predetermined phone line for retrieval. This is done from participants' usual practice sites, where there are daily routines, standard equipment, and usual background activities and noises. Recipients retrieve the name for interpretation from the fax or by listening to the voicemail (simulating the spoken communication of the name).

Participants are sent all of their materials along with a timeline of when to complete each portion of the simulation process. The voicemail and fax records can be checked by the simulation organizer to ensure that participants are following the agreed upon timetable. Where respondents do not complete the scheduled task by the agreed upon time, follow-up phone calls are made to remind them of their obligations. Findings are not affected by a few drop-outs because they are not included in the presented sample sizes or in the findings. Large numbers of respondents can be enlisted to minimize skewing and to represent a broad user experience.

Once they complete the transmission or reception of drug names, participants must complete a questionnaire about the name(s) they have processed. (See Sample Follow-Up Questions under data Collection within the Summary of Findings.)

All details of the simulation and questionnaire responses are to be tabulated and reported.

Summary of Findings

Data Collection

1) Performance of the ‘Look’ of the Name

All interpretations of written names are listed, correct and incorrect.

2) Performance of the ‘Sound’ of the Name

All interpretations of heard names are listed, correct and incorrect.

3) Sample Follow-Up Questions

- Does this name look like any other drug name?
- Does this name look like any other medical term or laboratory test?
- Does this name look like any other general product (non-medical)?
- Does this name sound like any other drug name?

- Does this name sound like any other medical term or laboratory test?
- Does this name sound like any other general product (non-medical)?

Table 2: Findings for *NAME*

Factor	Yes Responses	Findings and Comments
Does this name look like any other drug name?	5/15	There was a high risk of confusion with other drug names. Yet the only other drug names that respondents think look like <i>NAME</i> are AAA and <i>NAME</i> .
Does this name look like any other medical term or laboratory test?	1/15	There is low risk of confusion for other medical terms or laboratory tests, as the only mention was BBB.
Does this name look like any other general product (non-medical)?	1/15	There was a low risk of confusion for general products, with the one respondent thinking of CCC.
Does this name sound like any other drug name?	4/15	The risk of confusion is moderate for sounding like other drugs, associations again include AAA and <i>NAME</i> .
Does this name sound like any other medical term or laboratory test?	0/15	There was no risk of confusion with other medical terms or laboratory tests.
Does this name sound like any other general product (non-medical)?	1/15	The risk of confusion is low , the only general product association mentioned was DDD.

Table 3: Perceived Confidence and Safety of NAME

Scale: 1–10, where 10 indicates very confident/safe & 1 indicates not confident/safe.				
Factor	Mean Rating	Findings	High Scorer Comments	Low Scorer Comments
Pronunciation will be correctly understood via telephone or voicemail	8.1	High score indicates that there is low risk of medication errors when verbally saying/interpreting the name.	<ul style="list-style-type: none"> • <i>easy to say/pronounce</i> • <i>pronounced just as it's spelled</i> • <i>sounds unique</i> • <i>phonetically pleasing</i> • <i>short</i> • <i>not complicated</i> 	<ul style="list-style-type: none"> • <i>difficult to understand when pronounced</i> • <i>may be mispronounced</i> • <i>'aaa' may be heard as 'aai' or 'aga'</i> • <i>unsure of spelling</i> • <i>difficult name</i> • <i>too similar to BBB</i>
Will be legible when faxed or written	8.5	High score indicates that there is a low risk of errors when reading the faxed or written name.	<ul style="list-style-type: none"> • <i>spelled as it sounds</i> • <i>unique spelling</i> • <i>not similar to anything else</i> • <i>clear/easy to write</i> • <i>easy to read</i> 	<ul style="list-style-type: none"> • <i>difficult to spell</i> • <i>not sure of spelling</i> • <i>'aaa' may be confused with 'aai' or 'aga'</i>
Is safe, will not cause medication errors or confusion	8.4	High score indicates that this name is perceived as very safe.	<ul style="list-style-type: none"> • <i>sounds unique</i> • <i>not likely to be confused with anything else</i> • <i>easy to say/spell which will lead to no errors</i> 	<ul style="list-style-type: none"> • <i>too similar to other drugs</i> • <i>unclear sounding</i> • <i>hard to pronounce</i>

Table 4: Interpretation of Name in Simulation Process: NAME

Manner	Correct	Errors
Received via handwritten fax	1/2	AAA
Retrieved via voicemail	6/8	BBB, CCC
Received via typed fax	2/2	No errors
Total correct interpretations and commentary	9/12 (75%) Voicemail appears to pose the greatest problem as the verbal pronunciation can be interpreted in a couple of different ways, especially for a name that has not been seen before. The middle 'o' in the name was often confused as an 'i'. Exposure to the name via detailing and marketing may decrease this misinterpretation as the overall perception of the name in terms of saying and spelling it scores well.	

Appendix 5 – Additional Attributes to Assist in Determining the Degree of Similarity

Below, are additional examples of attributes to take into consideration in determining the degree of similarity of the proposed name during the FMEA process:

- Identical Prefix
- Identical Infix
- Identical Suffix
- Similar length of the name
- Similar spelling
- Upstrokes (capital and lower case e.g. 'P', 'd') in similar locations
- Downstrokes (e.g., 'q', 'y') in similar locations
- Cross-strokes (e.g., 'x', 't') in similar locations
- Dotted letters (e.g., 'i') in similar locations
- Ambiguity introduced when scripting letters (e.g., 'P' may appear as 'B', 'D', or 'R'; lower case 'r' may appear as 'e', 'v' or 'l'; lower case 'a' may appear as any vowel; lower case 'x' may appear as lower case 't', 'f' or 'y' etc.)
- Similar number of words/groups of characters in a name (A "word" is considered as any group of characters separated by a space)
- Similar number of syllables
- Similar stresses (e.g., Trycel and Triafil have similar stresses: TRY-cel and TRIA-fil; try-CEL and tria-FIL)
- Placement of vowel sounds is similar (e.g., 'e' may sound like 'a' or 'i'; 'i' may sound like 'a' or 'e'; 'a' may sound like 'e' or 'i' etc.)
- Placement of consonant sounds is similar (e.g., 'n' may sound like 'm', 'dn', 'gn', 'kn', 'mn', 'pn'; 't' may sound like 'd', 'b' or 'pt' etc.)
- First letter and/or sound (but made with the same letter) is identical
- Last letter is identical
- Same letters but in different order (e.g., Termix and Trevisc - the "er" and "re" can be interpreted as the same and do not provide protection from name confusion)

Appendix 6 - Failure Mode and Effects Analysis (FMEA)²⁷

Sample FMEA Process for Confusability of Health Product Names

Step 1: Select a topic to be analyzed and assemble a team.

The topic of the FMEA is Proposed Brand Name Confusability. The team includes representation from actively practicing healthcare practitioners and ancillary healthcare or non-healthcare staff, who would be involved in the product's use (e.g., nurses, pharmacists, pharmacy assistants, secretaries, clerks). The FMEA team includes active practitioners in the field of use for the product.

Step 2: Diagram the process to be analyzed.

Use the medication-use process map(s) developed for the product as part of the Simulate step (section 2.3.2.1).

The FMEA panel reviews the drug use process map(s), assesses their adequacy in describing the product's use, and, if necessary, adds additional transaction points, based on their expertise and experience with similar drugs or settings.

Step 3: Brainstorm potential failure modes within the process and identify their effects. What could go wrong?

The primary failure mode to be considered is the possibility that at any stage of the medication-use process **the product name or other attributes could result in confusion potentially leading to an error**. The effects resulting from name confusability, or confusion caused or contributed by non-name attributes are identified and discussed by the team.

The team must answer the following questions, considering the proposed name and the potentially confusable names, both identified through the Search and Simulate steps and generated by the FMEA team members. Rating of harm can be expressed using the National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) taxonomy of harm, A to I.

1. Are any of the drugs that could be confused with the proposed brand name:
 - a) a high alert drug or a drug with a narrow therapeutic index²⁸
 - b) a pharmacological opposite
 - c) a product with significant contraindications or warnings and precautions,
 - d) a product with known drug interaction or allergies
 - e) a product with a high prescribing frequency

2. Omitting the drug
 - a) What are the consequences of omitting the intended drug?
 - b) What would be the consequences of omitting the intended drug in special patient populations, e.g., patients who are very young, pregnant, elderly, nursing, or have compromised liver or kidney function?
 - c) How long could a patient go without the intended treatment before being adversely affected?

3. Wrong drug therapy
 - a) What are the consequences of being exposed to the wrong drug (i.e., all the confusable drug names identified in Search and Simulate steps and by the FMEA panel)?
 - b) What number of doses would need to be administered to cause harm?
 - c) What would be the consequences of receiving the wrong drug in special patient populations, e.g., patients who are very young, pregnant, elderly, nursing, or have compromised liver or kidney function?

4. Combined drug therapy
 - a) What are the consequences of combined drug therapy?
 - b) Is there a potential to exacerbate adverse reactions?

Step 4: Identify the causes of the potential failure modes. Why could things go wrong?

The primary cause for potential name confusion in this FMEA is the LASA/confusable drug name, as identified in the previous steps of the name review, Search and Simulate.

In addition to name confusability, and considering the findings of the real world simulations, the FMEA must assess the amount of overlap in non-name attributes of the proposed name and product and any potentially confusable existing names and products. These, at minimum, include marketing status (Rx or non-prescription), therapeutic category, medicinal ingredient(s), indication(s), clinical setting for dispensing/administration/use, strength, dosage form, route of administration, proposed dose, dosing interval/frequency, and storage (e.g., refrigerated or room temperature).

Step 5: Redesign the process/product to address the potential failure modes.

Reviewing the severity and detectability indicators, the team must identify the failure modes with the highest indicators. How to affect or mitigate these failure modes can then be considered in light of the proposed name and the product's non-name attributes. The goals are to prevent errors, to make errors more visible (preferably before reaching the user/patient), and to prevent harm to the user/patient.

It should be kept in mind that reliance on human memory and cognition are not true 'fixes', as they are dependent on individuals working under ideal circumstances with optimal resources and alertness.

References

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Additional Reading

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Endnotes

1. Health Products and Food Branch, Health Canada. Guidance for industry. Drug name review: look-alike sound alike (LA/SA) health product names [Internet]. Ottawa (ON): Minister of Public Works and Government Services Canada; 2005 [cited 2014 Jun 20]. Available from: http://www.hc-sc.gc.ca/dhp-mps/brgtherap/applic-demande/guides/drugs-drogues/lasa_premkt-noms_semblables_precomm-eng.php
2. Generic versions of products should contain the same modifier to the brand name version or innovator product to distinguish the different indications or dosing considerations, where permissible with respect to copyright/trademark law.
3. Guidance for Industry: Reconsideration of Final Decisions Issued for Human Drug Submissions: http://www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demande/guide-ld/revision-final/decisions_hum_drug_drogue-eng.php (cited: 2014 Jun 20)
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6. USAN Stem List: <http://www.ama-assn.org/ama/pub/physician-resources/medical-science/united-states-adopted-names-council.page> [cited 2014 Jun 20]
7. INN Stem List: <http://www.who.int/medicines/services/inn/en/> [cited 2014 Jun 20]
8. World health Organization. Guidance on the establishment of new INN stems: http://www.who.int/medicines/services/inn/stems_policy_explanation.pdf [cited 2012 Feb 15]
9. The use of colloquial abbreviations in a name may be misinterpreted. See abbreviations recognized as error-prone and potentially dangerous by the Institute for Safe Medication Practices (www.ISMP.org/tools/errorproneabbreviations.pdf [cited 2012 Feb 15]).
10. This would not be considered sufficient differentiation between two products of differing formulations and these single letters and digits are easily lost or confused with strength or dosage.
11. USAN Stem List: <http://www.ama-assn.org/ama/pub/physician-resources/medical-science/united-states-adopted-names-council.page> [cited 2014 Jun 20]
12. INN Stem List: <http://www.who.int/medicines/services/inn/en/> [cited 2012 Feb 15]
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14. Available from: <http://webprod5.hc-sc.gc.ca/dpd-bdpp/index-eng.jsp> [cited 2012 Feb 15]
15. Available from: <http://webprod3.hc-sc.gc.ca/lnhpd-bdpsnh/> [cited 2012 Feb 15]
16. A computer algorithm to measure similarity is the FDA's Phonetic and Orthographic Computer Analysis (POCA) software program, which has been released freely to the public and is available from commercial search vendors. <http://www.fda.gov/OHRMS/DOCKETS/98fr/E9-3170.pdf>
17. Available from: <http://www12.statcan.ca/census-recensement/2011/as-sa/98-314-x/98-314-x2011001-eng.cfm> [cited 2013 Dec 19]
18. Most medications have a moderate margin of safety, yet a small number of drugs have a high risk of causing injury when they are misused. These are called 'high-alert medications'¹⁹ to draw attention to this characteristic, and so all involved in their use will handle them with the care and respect they require. Errors may or may not be more common with the use of these drugs compared to others. However, the consequences of the errors are more devastating and their use requires enhanced precautions. These medications often need to be packaged differently, stored differently, prescribed differently, dispensed

differently and administered differently than most other medications. **Note:** Definition adapted from the Institute for Safe Medication Practices (ISMP) (http://www.ismp.org/faq.asp#Question_5 [cited 2012 Feb 15]).

19. ISMP's List of High-Alert Medications is available from: www.ismp.org/Tools/highalertmedications.pdf. The ISMP List of High-Alert Medications in Community/Ambulatory Healthcare is available from: <http://www.ismp.org/communityRx/tools/highAlert-community.pdf> [cited 2012 Feb 15]
20. Lebel M.J. Drug names and medication errors: Who is responsible? *Can Med Assoc J.* 1993;149(7):941-943.
21. Guidelines on the Use of International Nonproprietary Names (INNs) for Pharmaceutical Substances, 1997, Programme of International Nonproprietary Names, Division of Drug Management and Policies, World Health Organization, WHO/Pharm S/NOM 1570.
22. The terms label and labelling are used synonymously in this document and refer to inner and outer label.
23. Developed by the collaborating parties of the Canadian Medication Incident Reporting and Prevention System. 2001. Collaborating parties for the development and implementation of the Canadian Medication Incident Reporting and Prevention System (CMIRPS) are: Institute for Safe Medication Practices Canada, Canadian Institute for Health Information and Health Canada.
24. ISMP's List of Error-Prone Abbreviations, Symbols, and Dose Designations: www.ISMP.org/tools/errorproneabbreviations.pdf [cited 2012 Feb 15]
25. National Coordinating Council on Medication Error Reporting and Prevention: www.nccmerp.org [cited 2012 Feb 15]
26. Available from: http://www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demande/guide-ld/label_guide_ld-eng.php [cited 2014 Jun 20].
27. The Institute for Safe Medication Practices Canada has published an FMEA manual focused on process analysis, the *Canadian Failure Mode and Effects Analysis Framework. Proactively Assessing Risk in Healthcare.* 2007. Other sources of information and FMEA tools are available on-line from Resource Engineering, Inc. (<http://www.qualitytrainingportal.com/resources/fmea/index.htm>) and the American Society for Quality (<http://asq.org/learn-about-quality/process-analysis-tools/overview/fmea.html>) [cited 2012 Feb 15].
28. National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP). NCC MERP Taxonomy of Medication Errors. 1998. Section 30, Patient Outcome. Available from: www.nccmerp.org/pdf/taxo2001-07-31.pdf [cited 20 Feb 2012].