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Biologics and Genetic
Therapies Directorate
2nd Floor, Building # 7
Address Locator # 0702E
Tunney's Pasture
OTTAWA, Ontario
K1A 0L2

March 24, 2004

Stakeholders:

Subject: Issue Analysis Summary: Look-alike Sound-alike (LA/SA) Health Product Names: The Development of a Comprehensive Policy Recommendation

The purpose of this note is to inform you that following consultation with stakeholders and a careful review of comments received on the draft *Issue Analysis Summary Look-alike Sound-alike (LA/SA) Health Product Names: The Development of a Comprehensive Policy Recommendation* distributed and posted on our website in October 2003, Health Canada would like to announce that the attached final *Issue Analysis Summary Look-alike Sound-alike (LA/SA) Health Product Names: The Development of a Comprehensive Policy Recommendation* is now available and may be accessed from the Biologics and Genetic Therapies website at http://www.hc-sc.gc.ca/hpfb-dgpsa/bgtd-dpbtg/index_e.html.

For further information regarding this project, please contact:

Ms. Michèle Chadwick, Policy and Promotion Division, Centre for Policy and Regulatory Affairs, Biologics and Genetic Therapies Directorate, Health Canada, Tunney's Pasture, Address Locator:0702A, Tunney's Pasture, Ottawa, Ontario, K1A 0L2.

Email: michele_chadwick@hc-sc.gc.ca
Phone: (613) 946-5730
Fax: (613) 948-7598

Thank you for your interest in this issue.

Original signed by

Julia Hill
Director General

Enclosure

ISSUE ANALYSIS SUMMARY
Look-alike Sound-alike (LA/SA) Health Product Names:
The Development of a Comprehensive Policy Recommendation

Prepared by the LA/SA Working Group

Ms. M. Chadwick, Chair
Ms. M. Boudreau
Ms. V. Butz
Ms. J. Clare
Ms. J. Desrosiers
Ms. R. Hansson
Dr. D. Gaon
Dr. B. Ghosh
Ms. M. Ho
Mr. B. Leslie
Ms. G. Mah-Cawthorn
Ms. S. Pereira
Ms. K. Reinhard
Ms. M. Schwartz
Dr. S. Sharma
Mr. M. Wood
Ms. C. Yen
Ms. D. Yu
Ms. M. Zimmerman

Biologics and Genetic Therapies Directorate (BGTD)
Health Products and Food Branch (HPFB)
Health Canada

March 23, 2004

ISSUE ANALYSIS SUMMARY

Biologics and Genetic Therapies Directorate **March 23, 2003**

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EXECUTIVE SUMMARY

Look-alike sound-alike (LA/SA) health products refer to names of different health products that have orthographic similarities and/or similar phonetics (i.e. similar when written or spoken). These similarities may pose a risk to health by causing errors in prescribing, dispensing or administration of a product.

A specific safety issue involving the potential for confusion between two approved biologics, as well as long-standing unresolved issues relating to LA/SA health product names prompted the Biologics and Genetic Therapies Directorate (BGTD) to initiate a review and analysis of the issues associated with LA/SA health product names and to recommend an appropriate course of action.

The Health Products and Food Branch (HPFB) interdirectorate LA/SA Working Group (WG), with representation from Biologics and Genetic Therapies Directorate [BGTD (lead)], HPFB Inspectorate, Marketed Health Products Directorate (MHPD), Natural Health Products Directorate (NHPD), Therapeutic Products Directorate (TPD), Veterinary Drugs Directorate (VDD), Health Policy and Communications Branch and Legal Services was tasked with this project.

The LA/SA WG decided to focus specifically on LA/SA name issues that, based on current knowledge, appeared to pose the most potential for health risk. Priority issues included:

- similar brand names;
- brand names that are similar to generic names; and
- product line extensions.

After developing numerous pre- and post-market options, the LA/SA WG used quantitative and qualitative techniques to rank the various combination of options.

The LA/SA WG recommends that the 1st pre- and post-market choices be endorsed.

Pre-market, the LA/SA WG recommends that a complex computer application be acquired to screen for LA/SA health product names. Those names that are flagged as problematic should be reviewed and if the reviewer (process for assigning reviewer to be determined in the implementation phase) cannot reach a decision regarding the LA/SA name in question, it would be considered further by an Interdirectorate Name Review Committee (to be formed in the implementation phase). When filing a submission, a sponsor would be required to show that a proposed health product name does not have LA/SA name similarities. Furthermore, the sponsor would have the option of providing a prioritized list of name choices.

Post-market, the LA/SA WG feels that potential LA/SA health products should be monitored. If sufficient risk of harm due to potential medication errors is identified, appropriate market interventions should be initiated (e.g. Fact Sheets, Dear Health Care Professional Letters, name or labelling change to one of the products etc.).

The LA/SA WG proposes a phased implementation of the LA/SA policy where priority would be given to Schedule C, Schedule D, Schedule F and prescribed drugs for human use before over-the-counter, natural health products, veterinary drugs and medical devices.

Public involvement activities were undertaken and based on comments received, the document *Look-alike Sound-alike Health Product Names: Comments and Responses to the Issue as presented in the Issue Analysis Summary* was developed to respond to stakeholders' comments/questions. Of note, based on stakeholder feedback, this IAS has been revised.

It is anticipated that HPFB will move forward in implementing pre and post-market recommendations.

1. ISSUE

Look-alike sound-alike (LA/SA) health products refer to names of different health products that have orthographic similarities and/or similar phonetics (i.e. similar when written or spoken). These similarities may pose a risk to health by causing errors in prescribing, dispensing or administration of a product. These medication errors may be more likely to occur because of contributing factors such as identical doses, dosage forms or routes of administration, similar packaging or labelling, incomplete knowledge of drug names, illegible or unclear handwriting, verbal order errors (similar phonetics), orders that are confusing or incomplete, data processing errors, errors in documentation and even lack of appropriate knowledge base. A specific safety issue involving the potential for confusion between two approved biologic drugs for human use as well as long-standing unresolved issues relating to LA/SA health product names has prompted the Biologics and Genetic Therapies Directorate (BGTD) to initiate a review and analysis of the issues associated with health products and to recommend an appropriate course of action.

To date, only similarities in pharmaceutical, biological and veterinary drug names have resulted in documented LA/SA medication errors. There have been no recorded cases of LA/SA medication errors due to natural health products, or medical devices.

2. PURPOSE/OBJECTIVES

2.1 Purpose of Policy Development

The purpose of the policy development process is to develop options to respond to the issue of LA/SA health product names and make recommendations to BEC-Risk.

2.2 Objectives

A consistent and formal process is required within HPFB to address LA/SA health product names. Pre-market and post-market processes must be developed to respond to LA/SA issues of similar brand names (including the use of abbreviations or suffixes in brand names), brand names that are similar to generic names [International Nonproprietary Names (INNs) or United States Adopted Names (USAN)] and product line extensions. With a formal process in place, potential for medication errors due to LA/SA similarities should be reduced.

BGTD will take the lead in the inter-directorate development of a consistent and formal process within HPFB to review LA/SA aspects of health product names for Schedule C, Schedule D, Schedule F and prescribed drugs*.

*Prescribed drugs are neither over-the-counter products nor are they listed on Schedule F. Examples include potassium chloride for injection and dextrose injection.

2.3 Working Group

An interdirectorate LA/SA Working Group (WG) was established to develop policy recommendations for LA/SA health product names. It consists of the following members:

Michelle L. Boudreau, Legal Services

Vicky Butz, Submission and Knowledge Management, Veterinary Drugs Directorate, HPFB

Michèle Chadwick (lead), Policy and Promotion Division, Centre for Policy and Regulatory Affairs, BGTD, HPFB

Julie Clare, Submission Management Division, Centre for Policy and Regulatory Affairs, BGTD, HPFB

Julie Desrosiers (replaced Dominique Tremblay as of April 22, 2003), Strategic Communications and Planning Division, Marketing and Consultation Directorate, Health Policy and Communications Branch

Deborah Gaon, Clinical Evaluation Division, Veterinary Drugs Directorate, HPFB

Basanti Ghosh, Submission Management Division, Centre for Policy and Regulatory Affairs, BGTD, HPFB

Ruth Hansson (secretariat), Policy and Promotion Division, Centre for Policy and Regulatory Affairs, BGTD, HPFB

Micheline Ho, Product Information Division, Senior Medical Advisor Bureau, TPD, HPFB

Bill Leslie, Policy and Partnerships Division, MHPD, HPFB

Gloria Mah Cawthorn, Biologics and Radiopharmaceuticals Evaluation Centre, BGTD, HPFB

Kerry Reinhard, Bureau of Product Review and Assessment, NHPD, HPFB

Stephanie Pereira, Bureau of Product Review and Assessment, NHPD, HPFB (replaced Kerry Reinhard as of June 2, 2003)

Marilyn Schwartz, Submission and Information Policy Division, Bureau of Operational Services, TPD, HPFB

Supriya Sharma, Marketed Biological and Biotechnology Products Division, MHPD, HPFB

Michael Wood, Submission and Information Policy Division, Bureau of Operational Services, TPD, HPFB

Catherine Yen (replaced Marie Morrisey as of April 22, 2003), Compliance and Enforcement Division, National Coordination Centre, HPFB Inspectorate, HPFB

Deborah Yu, Bureau of Policy and Regulatory Affairs, NHPD, HPFB

Ms. M. Zimmerman, Patient Safety Section, Policy and Partnerships Division, MHPD, HPFB

3. BACKGROUND

Issues of LA/SA drug names are well documented in medical literature and within Health Canada. Name confusion is thought to account for one in every four medication errors[1] .

[1]B.L. Lambert, S.J. Lin, K.Y. Chang and S.K. Gandhi, "Similarity as a risk factor in drug-name confusion errors: the look-alike (orthographic) and sound-alike (phonetic) model," *Med Care*

Related statistics show that of the 25 000 medication error reports received by the FDA, 12.5% of errors are related to names[2]. Furthermore, a recent FDA study of 400 deaths caused by medication errors found that 5% of deaths were attributed to proprietary name confusion and 4% to generic name confusion. [3] It is reasonable to extrapolate these statistics to predict that the incidence medication errors in Canada are similar to that of the U.S., especially since may sponsors strive for global consistency in the branding of their products.

Within Health Canada, written records show that the long standing recurrent issue of LA/SA drugs date back to 1976 when Dr. Denise Leclerc-Chevallier (past Director, former Bureau of Drug Quality Assessment) expressed concern over three similar brand names. In response to this concern, it was mentioned that the subject of LA/SA drug names was well-known and there was little ability to exert control over enforcing changes to brand names based on the way subsection 9(1) of the *Food and Drug Act* reads.

Various stakeholders, including the Canadian Medical Association (CMA), Canadian Pharmacists Association (CPhA), the Canadian Society of Hospital Pharmacists (CSHP) and the Institute for Safe Medication Practices (ISMP), have been concerned about the LA/SA issue for a number of years.

More recently, it was brought to the attention of Health Canada (HC) by the Institute for Safe Medication Practices Canada (ISMP Canada) that LA/SA brand name similarities existed between two approved drugs for human use manufactured by the same sponsor. As a result, MHPD, following consultation with legal services and with input from HPFB senior management, notified the sponsor of their concerns and suggested that the sponsor change the name of one of the products or alternatively propose another solution to alleviate this potential safety risk. The sponsor decided to recall one of the products and the sponsor submitted an alternate name for the product that cleared as an administrative New Drug Submission (NDS).

Currently, LA/SA drug name issues are handled on a case-by-case basis. Since there is no consistent or formal process within the Branch to review LA/SA aspects of product names, the name review is somewhat arbitrary and depends on initiative, memory, intuition and judgement of staff. Current computer systems are not set up to flag identical or similar names. Furthermore, the subjective nature of similarities between drug names compounds the problem, since names that are similar to one person may not be to another. In addition, the general perception is that there is questionable authority as to whether the *Food and Drugs Act* can be used to require a name change. When a LA/SA drug is identified either pre- or post-market, the sponsor is notified and encouraged to consider changing their

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1999 Dec 37 (12): 1214-25.

[2]J. Phillips, "Look-Alike/Sound-Alike (LA/SA) Health Product Names Consultative Workshop", October 20-21, 2003: Proprietary Name Evaluation at FDA, Office of Drug Safety

[3]Lauran Neergaard, "FDA pushes to curb drug mix-ups," *The Boston Globe* (Associated Press) 2 Jan. 2002.

product name. Alternatively, they are questioned regarding any proposed remedial measures they can suggest to reduce the potential for medication errors. When such issues have been brought to the manufacturer's attention, HPFB success has been mixed. As a result, there is a general consensus that a long term strategy needs to be developed, in co-operation with stakeholders, to deal with LA/SA drug names.

Without a specific process in place and mixed results regarding the initial identification and subsequent action to resolve safety concerns regarding LA/SA health product names (i.e., compliance, monitoring and enforcement), a number of real and potential risks exist. These risks include:

- the morbidity and mortality of Canadians due to medication errors,
- the risk that public trust may be lost and the public perception may be that HPFB cannot adequately reduce the risk of harm to Canadians;
- a legal challenge based on arbitrariness when trying to act in accordance with the HPFB mandate, if decisions are made inconsistently; and
- HPFB's potential risk of liability for failure to meet responsibilities outlined in its mandate if beneficiaries of the program suffer morbidity and mortality due to medication errors.

With new drugs coming onto the market each year, the potential for LA/SA errors keeps growing. Dr. Bruce Lambert, an Assistant Professor of Pharmacy Administration at the University of Illinois (Chicago) states that to date there are 100 000 potential pairings of drug names that could be confused[4].

3.1 Definitions

Brand name: *C.01.001. 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.*

The use of a brand name is currently the choice of the sponsor. As stated in Section *C.01.004 (1) of the Food and Drug Regulations*, a drug is identified on its inner and outer label by the brand name (if there is one) followed by the proper name, if any. If there is no proper name, the common name is listed instead.

[4]Rob Waters, "The Perils of Prescriptions," *Shepherd Express Metro* 3 June 1999 Volume 20, Issue 23.

Chemical name: The chemical name of a drug 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-Chlorophenyl)-1-[3-(4-flurobenzoyl) propyl]-piperidin-4-ol: 4-[4-p-Chlorophenyl]-4-hydroxypiperidino]-4-flurobutyrophenone is the chemical name for Haloperidol}.

Common name: *C.01.001 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 publications referred to in Schedule B to the Act.*

Generic name: The generic or non-proprietary name describes the drug substance. INNs 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.

Health product: Health products include pharmaceuticals, biologicals, vaccines, medical devices, natural health products, radiopharmaceuticals and veterinary drug products.

International Nonproprietary Name (INN): INNs identify 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). An INN is the only internationally accepted generic name. In Canada, INNs are used exclusively, when they exist, in Schedule F.

Look-alike Sound-alike (LA/SA) health products: Health products that have a similar written name or similar phonetics to another health product.

Product line extension: A product line extension results when a drug is named by using the brand name of another drug with the addition of a modifying prefix or suffix that is intended to distinguish the new product from the original. This practice has arisen as a marketing strategy to take advantage of familiarity of an original product name.

Proper name: *C.01.001. 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.*

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.*

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): USANs identify 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.

3.2 Summary of LA/SA drug name information to date

A history of LA/SA drug name information was developed from LA/SA files received from BGTD, MHPD and TPD staff and former LA/SA WG members (a LA/SA WG existed in the early 1990's) who had previously been involved in the LA/SA drug name issue. In reviewing this information, it is evident that:

- the issue has been long-standing and recurrent;
- medication errors may be more likely to occur because of contributing factors such as identical doses, dosage forms or routes of administration, similar packaging or labelling, incomplete knowledge of drug names, illegible or unclear handwriting, verbal order errors (similar phonetics), orders that are confusing or incomplete, data processing errors, errors in documentation and even lack of appropriate knowledge base;
- there is significant under reporting of adverse drug reactions, including medication errors;
- resources have not been available to appropriately deal with the issue;
- the authority of HPFB [formerly Health Protection Branch (HPB)] to require changes to drug names has been repeatedly questioned internally;
- it has been stated repeatedly that there is not enough evidence of a sufficient health hazard to warrant committing resources to LA/SA drug names;
- stakeholders are looking to Health Canada to take a leadership role with LA/SA drug names;
- stakeholders have attempted to address problems with LA/SA drug names by

developing committees to alert HPFB and other stakeholders of LA/SA drug name issues;

- if there is non-voluntary compliance by drug sponsors, it has been suggested that HPFB obtain regulatory authority to enforce name changes;
- HPFB agrees, generally, that all parties are responsible and need to work together to ensure medication errors do not occur as a result of LA/SA drug names; and
- a number of ideas have been raised regarding LA/SA drug names but apart from the draft *Product Line Extension Policy*, they have not been developed further.

3.3 Past Policy Development

Although a number of draft policies (outlined below) have been proposed to deal with different aspects of LA/SA drug names, none are being applied. Of note, all policies refer specifically to drugs (not health products).

Draft policy regarding the use of abbreviations in brand names of drug products

In 1992, a draft policy entitled *Use of Abbreviations in Brand Names of Drug Products* was developed to address the use of abbreviations and suffixes in drug names.

The policy stated that abbreviations will normally be considered acceptable providing that:

1. The abbreviation reinforces, in a clear manner, existing statements on the label and aids the health professional in selecting the appropriate medication.
2. Prominence given to the abbreviation should reasonably equate to that given to the actual statement explaining the abbreviation.
3. The abbreviation should not be represented in such a way that it could be misinterpreted or cause an erroneous impression among health professionals.
4. The abbreviation should provide useful and easily identifiable information to the health professional.

A preliminary list of abbreviations was proposed. Currently, this draft policy is not being applied.

Draft policy regarding brand names that are similar to generic names

A 1992 draft policy (un-named) attempted to address the issue of brand name/generic name confusion, as well as reduce the possibility of impeding the development of new INNs, by considering that brand names for drug products would not be acceptable in the following

cases[5]:

1. The brand name cannot be identical to any INN.
2. The brand name cannot contain any word stem designated by the World Health Organization (WHO) as indicating a class of therapeutic substances.
3. The brand name cannot contain more than three identical letters of the alphabet in the same order as that contained in any INN exclusive of the word stem.

This draft policy is not being applied.

Draft policy regarding product line extensions

A draft policy entitled *Product Line Extensions in Drugs for Human Use* (April 25, 1995) was developed with initial input from the Drugs and Therapeutics Subcommittee at the Canadian Medical Association (CMA). This policy provides a guideline to assist sponsors in naming products within product lines. It states that a submission for a line extension may only be accepted if:

1. All products in the product line are in the same therapeutic class.
2. There is a principal medicinal ingredient common to all products in the line; and
3. The product name is sufficiently different to clearly distinguish it from other products in the line.

The consultation process undertaken, regarding this policy, did not lead to a consensus and the issue was put on hold due to competing priorities.

4. ISSUE IDENTIFICATION AND ANALYSIS

4.1 Issue Scope

The LA/SA WG identified the potential scope of the problem and decided, by consensus, to focus specifically on LA/SA issues that, based on current knowledge, appear to pose the most potential for health risk.

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[5]Michael J. LeBelle, "Drug names and medication errors: Who is responsible?" *Can. Med. Assoc. J.* 1993; 149 (7), 941-943.

Of note, the LA/SA WG unanimously agreed to deal with each priority issue separately. If a problem develops with one priority issue which could result in delays, the other priority issues can continue to progress towards a recommendation and solution.

The priority issues of the LA/SA WG are:

- Similar brand names (including the use of abbreviations or suffixes in brand names).
- Brand names that are similar to generic names.
- Product line extensions.

Issues of lower priority that may be dealt with at a later date include:

- Generic name similarities.
- Similar brand name sub-issue - creating brand names by adding company abbreviations as a prefix to a different generic name (i.e. Apo Chlorpropamide, Apo Chlorpromazine).

The LA/SA WG has decided that the following issues are not within the scope of the WG:

- Similar brand name sub-issue - creating brand names by adding company abbreviations as a prefix to the same generic name (i.e. PMS-Amoxicillin, GEN-Amoxicillin).
- Similarities in labelling or packaging.
- Brand/generic name products prescribed by using abbreviations (i.e., AZT).

The LA/SA WG has decided that the following are not issues:

- Different brand names for the same active ingredient [within the same company (i.e. Wellbutrin, Zyban)].

LA/SA WG Decisions for Priorities

Brand name similarities

As brand name confusion was the primary reason for forming the LA/SA WG, the issue of similar brand names is considered to be a priority. The LA/SA WG has also agreed to review

the use of abbreviations or suffixes in brand names because the perceived chance of confusion and/or error is higher when abbreviations are included in brand names. It is also believed that this problem may be getting larger because the incidence of abbreviations/suffixes in new product names is increasing.

It was decided that the similar brand name sub-issue of "creating a brand name by adding company abbreviations as a prefix to a different generic name" is not considered to be a great risk at this time.

The practice of "creating brand names by adding company abbreviations as a prefix to the same generic name" is not a priority, since there is no significant safety concern if a consumer receives the same medicinal ingredient with an alternative brand name.

Brand names similar to generic names

The LA/SA WG believes that the issue of "brand names similar to generic names" is a priority. The LA/SA WG agreed that it is important to be consistent with international bodies to ensure that brand names not be similar to nonproprietary names as the practice may lead to confusion and may even impede the development of new INN or USAN names.

Product line extensions

The LA/SA WG agrees that the issue of product line extensions is a priority as is the sub-issue of marketing products with same brand names yet different active ingredients. The LA/SA WG believes that product line extensions occur more often with new products and the perceived chance of confusion and/or error is high.

Similar generic names[6]

The LA/SA WG considered the issue of similar generic names and believes that preventive measures could be implemented to reduce errors between similar generic drugs (i.e., the use of capital letters in the middle of words on labels to emphasize that portion of the word). As Health Canada does not have much influence on requiring a change to international generic names (INNs, USAN names), this issue will be a secondary priority. It was noted that aspects of generic name similarities may be indirectly dealt with, since priority LA/SA issues may be applicable to generic name similarities.

[6]LeBelle, 941-943.

Similar proper/common names for the same active ingredient

Occasionally, a sponsor will choose not to name their product with a brand name and as a result, the proper and/or common name of the product will have the same or similar name to a product with the same active ingredient. In addition, when a product does have a brand name, a prescriber may choose to refer to the product by its generic name instead of the brand name. In either case, the LA/SA WG decided that this practice does not result in a LA/SA error. As a result, the LA/SA working group will not be focussing efforts on this issue.

Similarities in labelling or packaging

The LA/SA WG agreed that products with similarities in labelling and packaging only (no name similarities) fall outside the scope of the LA/SA issue.

Brand/generic names prescribed by using abbreviations

The LA/SA WG decided that this issue is outside the scope of the LA/SA WG and the jurisdiction of HPFB. It is an issue to be dealt with by the provinces and territories, physicians, pharmacists or their associations.

Different brand names for the same active ingredient (within the same company)

The LA/SA WG agreed that since different brand names for the same/similar active ingredient often occurs between companies and is unavoidable, the issue of different brand names for the same active ingredient within the same company is not significant. In addition, there is not much evidence to suggest that there is necessarily a significant health risk if such an error does occur. As a result, the LA/SA WG will not be focusing efforts on this issue.

4.2 Regulatory Considerations

Food and Drug Regulations (Part C-Drugs)

Pre-market

The *Food and Drug Regulations* require that a drug's name be provided in a drug submission as part of the information required to assess the safety and effectiveness of a product (refer to sections C.08.002. and C.01.014. of the *Food and Drug Regulations*).

Specifically, subsection C.08.002.(2) (b) of the *Food and Drug Regulations* state *(2) A new*

drug submission shall contain sufficient information and material to enable the Minister to assess the safety and effectiveness of the new drug including the following: (among other items)

(b) a statement of the brand name of the new drug or identifying name or code proposed for the new drug;

and

Subsection C.01.014.1 (2) (f) states that*: (2) An application under subsection (1) shall be made to the Director in writing and shall set out the following information: (among other items)*

(f) the brand name under which the drug is to be sold;

In addition, sub*section C.01.014.2 (2) (b)* states that: *(2) Where the Director believes on reasonable grounds that a product in respect of which an application referred to in section C.01.014.1 has been made (b) is a drug but that its sale would cause injury to the health of the consumer or purchaser or would be in violation of the Act or these Regulations, he may refuse to issue the document referred to in subsection (1).*

In summary, the LA/SA WG believes that the *Food and Drug Regulations* allow HPFB to adopt a pre-market requirement that the names of drugs not be confusing with one another [see subsection C.08.002.(1), C.08.002.(2), C.08.002.(3) and C.01.014.1(2) of the *Food and Drug Regulations*]. If confusion with another drug name was considered likely and confusion could result in safety concerns, then HPFB could refuse to issue a DIN (new drugs and drugs other than new drugs) and/or NOC (new drugs only), as applicable.

Post-market

Section C.01.013. of the *Food and Drug Regulations* requires that, upon request, a manufacturer must submit sufficient evidence by a specified date to establish the safety and effectiveness of a drug for the purposes recommended. When sufficient evidence is not provided, further sales of the drug can be suspended.

Upon becoming aware of a safety concern associated with LA/SA name confusion following issuance of an NOC and/or DIN for a drug, the LA/SA WG is of the opinion that HPFB can use C.01.013. to require the manufacturer to establish the safety of the drug under its recommended uses in light of a safety concern identified in relation to its name. If sufficient evidence is not provided, HPFB could consider suspending sales of the drug by way of the C.01.013 process.

Trade-marks Act

In Canada,

- health product names are not required to have trade-marks;
- trade-marks are not subject to regulation in the marketplace (e.g., Industry Canada might refuse registration of a trade-mark but they cannot refuse the use of the name in the marketplace); and
- similar trade-marks will be granted if one company proposes two trade-marks that are similar and that company intends to own both trade-marks.

As such, the Trade-Mark Act is not useful in eliminating look-alike sound-alike names in health products.

Of note, granting of a trade-mark does not necessarily entitle the holder of the registered trade-mark to use the name. In the case of drugs, the right to use is only granted by HPFB upon issuance of a DIN and/or Notice of Compliance, as applicable. As a result, HPFB can simply enforce the safety standards as required under the Food and Drugs Act without regard to which manufacturer may ultimately be entitled to use a particular name as a matter of trademarks law.

Trade Law

Pre-market

The working group has concluded that HC's refusal to authorize the sale of a proposed drug based on potential LA/SA similarities that could result in safety concerns should not pose concerns regarding international legal agreements under the *Marakesh Agreement Establishing the World Trade Organization* (WTO agreements) and the *North American Free Trade Agreements (NAFTA),* assuming that rational, objective and non-discriminatory criteria are developed and applied to respond to these situations.

Post-market

Based on WTO agreements and NAFTA, the WG recommends that HC should consider all other less "trade restrictive" options before moving to request a sponsor to change a drug name and/or stop sale of the drug. As with, the pre-market case, rational, objective and non-discriminatory criteria should be developed and applied to respond to these situations.

4.3 International Perspective

Food and Drug Administration (FDA) and its response to look-alike sound-alike proprietary product names

Over the past decade, the FDA has attempted to minimize medication errors attributed to look-alike sound alike drug names. The FDA considers the review of a proprietary name to be an important part of the review of any new application[7]. FDA officials have stated that the "FDA must do everything within its authority to maximize the likelihood that approved products will be used correctly in the real world" (Peter Honig, M.D.) and "FDA's goal is to try and catch the potential for error before the product is marketed"(Sharon Smith Holston, FDA's Deputy Commissionaire for External Affairs).

Two of the five factors in the implementing regulations of the Food Drug and Cosmetic Act (Act) that could make the labelling for a drug misleading[8] relate to LA/SA issues. They are:

- The employment of a fanciful proprietary name for a drug or ingredient in such a manner as to imply that the drug or ingredient has some unique effectiveness or composition when, in fact, the drug or ingredient is a common substance, the limitations of which are readily recognized when the drug or ingredient is listed by its established name.

- Designation of a drug or ingredient by a proprietary name that, because of similarity in spelling or pronunciation, may be confused with the proprietary name or the established name of a different drug or ingredient.

In determining whether the degree of similarity in spelling or sound of names may be problematic, a number of potential contributing factors are taken into consideration during review (i.e. dosage forms and/or routes of administration).

Apart from LA/SA names, there are other naming factors that appear to increase the

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[7]Dr. J Jenkins, Director of the Office of New Drugs, CDER, "Proprietary Names and the Drug Approval Process". *Proc. of Evaluating Drug Names for Similarities: Methods and Approaches Public Meeting.* Washington D.C. , June 26, 2003.

[8] "Review of CBER Regulated Product Proprietary Names. Appendix 2: Criteria for Review of Biological Product Proprietary Names," *Manual of Standard Operating Procedures and Policies, General Information Review. SOPP 8001.4 Version #1*, 15 Aug. 2002, U.S. Food and Drug Administration, Center for Biologics Evaluation and Research, 9 Jan. 2003 <http://www.fda.gov/cber/regsopp/80014app2.htm>.

possibility of medication errors[9]. They include the following:

- Different proprietary names for the same active ingredient

  Products with different proprietary names for the same active ingredient are avoided because safety concerns may arise if:

  (a) products with two different proprietary names but the same active ingredient are concomitantly prescribed, or

  (b) a patient is allergic to an active ingredient but unknowingly takes it because the product has a different proprietary name.

- Product line extensions

  Using the same name for a drug containing none of the same active ingredients as the original would likely not be approved because it has the potential for confusion.

- USAN names in proprietary names

  The use of USAN stems in proprietary names is avoided because it may create confusion in differentiating a drug's proprietary name from a common or established name. In addition, such use has the potential to limit selection of new USAN names.

The review of proprietary names begins during Phase II of an Investigational New Drug Submission (IND) and when a New Drug Application/Abbreviated New Drug Application (NDA/ANDA) is filed[10]. The process includes an expert panel review, handwriting and verbal analyses, computer-assisted analysis, labelling and packaging analysis and an overall risk evaluation (Appendix A).

In accordance with the FDA's recent concept paper "Premarketing Risk Assessment", the FDA is encouraging sponsors to submit a risk assessment and evaluation to support the safety of a proprietary trade name. This suggestion has been advocated by the Institute of Medicine in its December 1999 report "to Err is Human" and recommended by the Health and Human Services Advisory Committee on Regulatory Reform (November, 2002).

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[9]Dr. J Jenkins, Director of the Office of New Drugs, CDER, "Proprietary Names and the Drug Approval Process". *Proc. of Evaluating Drug Names for Similarities: Methods and Approaches Public Meeting.* Washington D.C. , June 26, 2003.

[10]T. G. Phillips, "DMETS Evaluation of Proprietary Names", *Proc. of Evaluating Drug Names for Similarities: Methods and Approaches Public Meeting.* Washington D.C. , June 26, 2003.

The FDA monitors all post-market reports of medication errors that are related to naming, labelling and packaging of drug products. Each report is classified for severity, type and cause of error. If appropriate, the FDA makes specific recommendations to the appropriate reviewing divisions regarding changing the labelling, packaging or proprietary name. If needed, the FDA will work with the sponsor to correct the problem by making a change in the packaging, labelling or name.

The FDA is working on a proposal that will require bar coding on all prescription medications[11]. Initially, bar-coding would be used on an inpatient basis but will eventually be applied to increase the accuracy of dispensing on an outpatient basis. Ultimately, physicians will be able to generate computerized prescriptions containing bar codes that, when received by a pharmacist, can be recorded electronically. The pharmacist would then select the desired product from the shelf and scan the bar code of the product which would be linked to the electronic record of the prescription order.

The FDA plans to modify its Adverse Event Reporting System (AERS) by incorporating a Taxonomy of Medical Errors to enhance its ability to detect medication errors, including look-alike sound-alike medication errors. This taxonomy will allow the staff to perform trend analysis based upon the numerous causes and types of medical errors, which is currently not available through AERS.[12]

Currently, the division is also working on four documents for industry that include[13]:

1. a policy and procedures manual with the purpose of minimizing medical errors[14],
2. a guidance document on the FDA process for submitting proprietary names for evaluation,
3. a guidance document outlining how to safely label and package drugs, and
4. a guidance document outlining Industry's role in evaluating a new proprietary drug

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[11]Mary Gross, Office of Drug Safety, "CDER, Bar Coding Human Drugs and Biologics-A Regulatory Initiative". *Proc from the 38th Annual Drug Information Association Meeting*, Chicago, Illinois, June 16-20, <http://www.fda.gov/cder/present/DIA62002/gross/sld001.htm>

[12]Office of Drug Safety Annual Report 2001, Center for Drug Evaluation and Research, Food and Drug Administration.
<http://www.fda.gov/cder/Offices/ODS/AnnRep2001/annualreport2001.htm>

[13]Guidance Agenda: Guidances CDER is Planning to Develop During FiscalYear 2003, http://www.fda.gov/cder/guidance/guidance-agenda.htm

[14]P.E. Clarke, "Resources to track and reduce medication errors increased", *CDER News along the Pike*, Vol. 8, Issue 2, July 24, 2002. <http://www.fda.gov/cder/pike/janfeb2002.pdf>

name[15].

The first two of these documents will be posted on the CDER website in the near future.

European Agency for the Evaluation of Medicinal Products (EMEA)[16]

As part of the EMEA's role in evaluating the safety of medicinal products, it is obliged to consider whether the proposed invented name (brand name) of the medicinal product could create public health concerns or potential safety risks. The EMEA attempts to ensure that a medicinal product's brand name cannot be confused with another health product, since this could raise safety issues if the prescription/medical instruction is misinterpreted.

Within the document entitled, the EMEA states that it is crucial (a) a transparent procedure for checking the acceptability of proposed brand names is operated, and (b) consistent, non-arbitrary criteria are applied when reviewing the acceptability of proposed brand names.

The EMEA believes that a brand name of a medicinal product should not be liable to cause confusion in print, handwriting or speech with the brand name of an existing medicinal product. If an objection is raised, it is evaluated taking into account other potentially distinguishing features including the pharmaceutical form, the route of administration, indication, condition of supply (prescription versus "over-the-counter") and new pharmaceutical forms and/or routes of administration. After assessing all the above-mentioned factors as a whole, the EMEA will decide whether or not the invented name of the medicinal product creates a potential safety risk.

The EMEA advocates and supports the World Health Organization (WHO) recommendations that brand names not be derived from International Nonproprietary Names (INNs) and that INN stems not be used in brand names.

The EMEA has reached a consensus amongst National Authorities in establishing principles to be applied to invented names of medicinal products processed through the EMEA centralized procedure. To date, the following principles have been agreed upon and are applied regarding LA/SA issues:

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[15]T. G. Phillips, "DMETS Evaluation of Proprietary Names", *Proc. of Evaluating Drug Names for Similarities: Methods and Approaches Public Meeting.* Washington D.C. , June 26, 2003.

[16]Committee for Proprietary Medicinal Products (CPMP), "Guideline on the Acceptability of Invented Names for Human Medicianl Products Processed through the Centralized Procedure",Revision 3, January 2002, The European Agency for the Evaluation of Medicinal Products, Human Medicines Evaluation Unit.

1. The invented name should preferably consist of only one word and should avoid qualification by letters or numbers. The use of short qualifications/abbreviations which do not carry an established and relevant meaning to all Membered States is unacceptable.

2. For the medicinal product containing a prodrug (a compound that is transformed in the human system into the same active substance of a related drug by chemical or metabolic means) a different invented name from the invented name of the medicinal product containing the related active substance is required.

The EMEA suggests that invented names be submitted as early as 12 months and, at the latest, 4-6 months prior to the planned submission date of the marketing authorization application. Up to three invented names can be proposed, in order of preference, per marketing authorization application, in order of preference. Furthermore, the EMEA requires that proposed drug names differ from existing names by at least three letters.[17]

The proposed invented names are provided to Member States for comment. In the event that the EMEA decides to object to the invented name, the sponsor has an opportunity to comment.

New Zealand (Medsafe)

The New Zealand Regulatory Guidelines for Medicines states that the proposed proprietary name for a new medicine or related product must not be, or likely to be, confused in any way in print, handwriting or speech with another medicine or related product currently registered in New Zealand[18].

Australia [Therapeutic Goods Administration (TGA)]

The TGA has no current guidelines or systematic process in place regarding LA/SA health products, however, the TGA is well aware of this issue. Organizations external to TGA (the Australian Pharmaceutical Advisory Council and the Medication Safety Working Party of the

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[17]D. A. Propp, "Sound-alike Look-alike Drugs: An Overdue Opportunity to Reduce Medical Errors," published correspondence within *Academic Emergency Medicine* Vol. 7 (Nov 2000): 1334-1335.

[18]"Guidance notes for Applicants for consent to distribute new and changed medicines and related products", *New Zealand Regulatory Guidelines for Medicines, Volume 1, 5th Edition,* October 2001. Medsafe, New Zealand Medicines and Medical Devices Safety Authority.

Council of Safety and Quality Health Care) that include, among others, pharmacists and consumers, that are devoting considerable attention to this issue and are pressing the TGA to make improvements in this area.

Japan

Japan's Health, Labour and Welfare Ministry has plans to compile an online database of medicine names and packaging, in an effort to curb the growing number of cases involving mix-ups of drugs that look alike. With this database, the Ministry hopes to monitor medicines and, if necessary, require sponsors to change the name or design of their product.

Other Regulatory Agencies

Based on research to date, no other regulatory agencies have any current processes/policies or guidelines posted on their websites regarding LA/SA health product names.

4.4 Individual Differences

Individuals pronounce and print words in different ways, whether it be due to individual writing styles or speaking differences. As such, these individual differences should be taken into account when considering options for LA/SA health product names.

5. OPTIONS ANALYSIS

Pre- and post-market options for LA/SA health products are outlined below.

It was noted that all pre- and post-market options could potentially apply to:

a. Similarities in brand names (including same brand name);

b. Brand names similar to generic names; and

c. Product line extensions.

5.1 Proposed Options (Appendix B)

Options	
Pre-market	Post-market
General ▸ Status Quo	General ▸ Status Quo

Policy ▸ SOP/Policy /Guideline ▸ Regulations/Legislation Computer related ▸ use of current Drug Submission Tracking System (DSTS)* ▸ use of current integrated Records Information Management System (IRIMS)** system ▸ development of new computer application in-house ▸ basic computer application ▸ LA/SA-specific complex computer application with added features Review process ▸ Foreign Review (FDA) ▸ Review by Third Party ▸ Name review (HC) ▸ Name review committee Sponsor filing requirements ▸ Sponsor provides a prioritized list of name choices ▸ Sponsor does search/analysis for LA/SA similarities ▸ Require trademarks Other ▸ Combination of options	Policy ▸ SOP/Policy /Guideline ▸ Regulations/Legislation Computer related ▸ Bar coding - product ID and verification ▸ electronic prescribing (printed scripts) Industry Requirements ▸ require company to change name of the health product ▸ require company to modify label (i.e. lettering on label) Monitoring (environmental scans) ▸ Incorporate LA/SA errors into ADR reporting ▸ LA/SA error reporting (from other jurisdictions)- look back (i.e. Anonymous FDA-MedWatch reporting) ▸ Foreign reviews ▸ ISMP-watchdog ▸ use pre-market system to look for LA/SA approved health products Health promotion/stakeholder awareness ▸ increase awareness of documented LA/SA health products to stakeholders (e.g. info line, fact sheets, Dear Health Care Professional Letters, comments in ADR newsletter, LA/SA website, education of LA/SA health products in medical schools) Other ▸ Combination of options

* The Drug Submission Tracking System (DSTS) is an internal system (circa 1994) that is used to record and track drug submission information.

** iRIMS^{TM} is an internal computer application used as a filing system by Central Registry who manage files for the HPFB.

5.2 Criteria Used to Assess Options

The LA/SA WG agreed to use both a quantitative and qualitative approach to assess options. The quantitative analysis included the use of a decision analysis technique to review options,

whereas the qualitative technique required that the LA/SA WG members vote on preferred options. It was agreed, at the outset, that these exercises would be used as a tool to facilitate discussion of the options and would not necessarily bind the group to selecting/adopting the preferred option it produced.

Quantitative Analysis

The LA/SA WG identified criteria to be used to assess options and grouped them into either screening criteria (must haves) or comparative criteria (nice to have). The results of this exercise are listed below:

Screening Criteria

- systematic;
- objective;
- non-biased/non-discriminatory;
- sustainable in the long term;
- contains a pre- and post-market solution;
- includes a computer application;
- HC has final say in the review decision;
- risk/benefit built into process; and
- flexibility in final course of action.

Management indicated that they would like the LA/SA WG to consider solutions that could be implemented with current tools as well as those that could require capital expenditures. In order not to screen out those options, the screening criteria "sustainable in the long term" had to be removed from the screening criteria list.

Comparative Criteria

- cost/benefit;
- minimal use of guidance/directives/policies;
- respect "Cabinet Directive on Law-Making" and "Regulatory Policy" in that non-legislative measures need to be considered prior to legislative measures;
- shared responsibility (sponsor involved in assessing name);
- minimize potential appeals;
- simple/least complex solution;
- timeliness for implementation of option; and
- timeliness to decision (on the proposed name of each health product).

A number of options that would not meet the screening criteria, even in combination with

other options, were eliminated from further consideration. Options that were removed included:

- Status quo (pre- and post-market):
- Foreign Review;
- Review by a third party; and
- the requirement for trade-marks.

The second part of the quantitative exercise involved the following steps:

- the LA/SA WG assigned a weight (between 1 and 10) to the comparative criteria according to its importance relative to other comparative criteria (i.e. a higher number reflects a greater weight);
- the LA/SA WG ranked options (using a 10 point scale) according to how well each option met each comparative criteria (i.e. a higher number reflects a greater ranking);
- each option's weighted score for each criterion was multiplied by the assigned weight of that criterion and then added to the other criterion scores to obtain overall scores for each option; and
- the option with the highest score became the top choice.

It was acknowledged that the final recommendation will have to involve a combination of options, as no single option satisfies all screening criteria. The LA/SA WG leader took criterion scores of the individual options and ranked the various combinations of options based on numbers provided by the LA/SA WG in the earlier exercise. The data and results of these scores were provided to the LA/SA WG for comment.

The options analysis exercise described above yielded the following options, in order of preference:

Leading pre-market LA/SA Options Ranking using Decision Analysis

option	**score**
Policy/Complex Computer Application /name review/name review committee/company provides name analysis and prioritized list	414
Policy/Complex Computer Application/name review/name review committee/company provides name analysis	409.6

Policy/Basic Computer Application/name review committee/company provides name analysis and prioritized list	408.8
Policy/Basic Computer Application/name review committee/company provides name analysis	404.4
Policy/DSTS/name review/name review committee/company provides name analysis and prioritized list	392.4
Policy/Basic Computer Application/name review/name review committee/company provides name analysis and prioritized list	391.2
Policy/Complex Computer Application/name review committee/company provides name analysis and prioritized list	390.8

Leading post-market LA/SA Options Ranking using Decision Analysis

option	**score**
policy	330
promotion	242.6
promotion and monitoring	234.6
change appearance of name	184
sponsor changes name	156.2
electronic Rx	136
bar coding	130

Qualitative analysis

The qualitative exercise required regular LA/SA WG members to select their top three LA/SA options [1 being the first choice (10 points), 2 being the second choice (5 points) and 3 being the third choice (2 points)]. LA/SA WG members were also required to select any complementary and post-market options that they felt should be implemented in addition to their chosen LA/SA options (Appendix C).

In order to consider solutions that could be implemented with current tools, LA/SA WG members were asked to choose the option they preferred that could be implemented in the

short term.

In order to limit the potential pre-market options in the qualitative exercise to a reasonable number, options were chosen from those that were most feasible/reasonable. Since it appears that there is existing regulatory authority to consider a product name when considering safety and efficacy, all regulatory options were removed from the qualitative list. Any options that gave "value added only" to a potential recommendation could be chosen by LA/SA WG members to complement their choices.

The LA/SA WG acknowledged that, at this time, the following post-market options are not as feasible, since they are perceived as being a significant burden to stakeholders:

- require the Sponsor to Change Name of the Health Product;
- require Sponsor to Modify the Label of the Health Product;
- bar coding; and
- electronic prescribing (printed scripts).

The results of this qualitative exercise are listed below:

option	**1st**	**2nd**	**3rd**	**score**
Policy/Complex Computer Application/name review/name review committee	6		1	62
Policy/Complex Computer Application /name review committee	3	3		45
Policy/Basic Computer Application/name review committee	2	2	2	34
Policy/Basic Computer Application/name review/name review committee	1	4	1	33
Policy/Build internal system/name review committee		1	3	11
Policy/Build internal system & name review/name review committee			5	1
Policy/DSTS system, name review, name review committee		1		5
Policy/Basic Computer Application/name review committee		1		5

Only three of the twelve LA/SA WG members chose options that could be implemented with current tools. All three suggested that the option "Policy/DSTS/name review/name review committee/company" was the favoured choice. Upon further discussion at the LA/SA WG meeting it was agreed that, in order for this option to be feasible, it would have to be supported with a Drug Product Database (DPD) search (web-based version) as the DSTS database only includes products marketed since the beginning of 1994 onward.

Note: The Drug Product Database contains product specific information on drugs approved and marketed for use in Canada. The database is managed by Health Canada and includes human pharmaceutical and biological drugs, veterinary drugs and disinfectant products.

options that can complement those above	
Sponsor provides a prioritized list of name choices	8 / 12
Sponsor does search/analysis	11 / 12

post-market options	
Policy	8 / 12
monitoring & promotion	9 / 12
Promotion	1 / 12

<u>Leading pre-market LA/SA Options Ranking using quantitative (decision analysis) and qualitative techniques</u>

option	**quantitative score**	**qualitative score (without company providing list and prioritized list)**
Policy/Complex Computer Application /name review/name review committee/company provides name analysis and prioritized list	**414**	**62**
Policy/Complex Computer Application/name review/name review committee/company provides name analysis	**409.6**	**62**
Policy/Basic Computer Application/name review/name	**408.8**	**33**

review committee/company provides name analysis and prioritized list		
Policy/Basic Computer Application/name review committee/company provides name analysis	**404.4**	**34**
Policy/DSTS/name review/name review committee/company provides name analysis and prioritized list	**392.4**	**5**
Policy/Basic Computer Application/name review/name review committee/company provides name analysis and prioritized list	**391.2**	**33**
Policy/Complex Computer Application/name review committee/ company provides name analysis and prioritized list	**390.8**	**45**
Policy/Build internal system & name review and name review committee/ company provides name analysis and prioritized list	**381**	**10**
Policy/Build internal system and name review committee/ company provides name analysis and prioritized list	**363**	**11**
Policy/Basic Computer Application/ name review	**377.6**	**5**

6. RECOMMENDATIONS

Pre-market

1st choice: Policy/Complex Computer Application/name review/name review committee/company provides name analysis and the option of providing a prioritized list

2nd choice Policy/Basic Computer Application/name review/name review committee/company provides name analysis and the option of providing a prioritized list

3rd choice Policy/Build internal system & name review and name review committee/ company provides name analysis and the option of providing a prioritized list

The preferred option that can be implemented without the purchase of a computer application.

Policy/DSTS system (enhanced with some DPD support) & name review and name review committee/ company provides name analysis and optional prioritized list

Post-market

1st choice Policy/Promotion & Monitoring

2nd choice Policy/Promotion

The LA/SA WG proposes a phased implementation of the LA/SA policy where priority would be given to Schedule C, Schedule D, Schedule F and prescribed drugs* for human use before over-the-counter, natural health products, veterinary drugs and medical devices.

*Prescribed drugs are neither over-the-counter products nor are they listed on Schedule F. Examples include potassium chloride for injection and dextrose injection.

The LA/SA WG recommends that their 1st pre- and post-market choices be endorsed.

Pre-market, the LA/SA WG recommends that a complex computer application be acquired to screen for LA/SA health product names. Those names that are flagged should be reviewed and if the reviewer cannot come to a decision, it is considered further by an Interdirectorate Name Review Committee. Prior to filing a submission, a sponsor would be required to show that a proposed health product name does not have LA/SA name similarities. Furthermore, the sponsor would have the option of providing a prioritized list of name choices.

Post-market, the WG feels that potential LA/SA health product names should be monitored and, if sufficient risk of harm due to potential medication errors is identified, appropriate market intervention should be initiated (e.g. Fact Sheets, Dear Health Care Professional Letters, name or labelling change to one of the products etc.). Based on WTO agreements and NAFTA, the WG recommends that HC consider less "trade restrictive" market interventions before moving to request a sponsor to change a drug name and/or stop sale of the drug.

In summary, the first priority is to implement both the pre-market and post-market option (ideally 1st choices) for Schedule C, D and F drugs, as well as prescribed drugs for human use as they pertain to:

- Similar brand names (including the use of abbreviations or suffixes in brand names).
- Brand names that are similar to generic names.
- Product line extensions.

From there, pre- and post-market options will be developed for over-the-counter drugs,

natural health products, veterinary drugs (including veterinary drug names that might be confused with human drug names) and medical devices, as required.

7. PUBLIC INVOLVEMENT

Public involvement activities have been undertaken in support of the development of a comprehensive policy recommendation for LA/SA health product names. Specifically, the objectives of the public involvement process have been to inform and educate stakeholders regarding LA/SA health product names and current policy development to date, to seek stakeholder feedback to ensure accuracy and completeness of the issues, options and proposed recommendations.

The stakeholder profile, or affected population, consists of the federal government (mainly Health Canada but could include others such as Industry Canada, Canadian Institute for Health Information), sponsors, pharmacists, healthcare professionals, professional health associations, non-governmental associations, consumer groups and patient advocacy groups.

To date, LA/SA consultation activities have included:

- presentations to management committees of affected directorates;
- consultation with the HPFB Advisory Committee on Management on October 1, 2003;
- the LA/SA consultative workshop held October 20, and 21, 2003 (Château Cartier Resort, Gatineau Québec) with stakeholders representing industry, government, healthcare professionals and non-government organizations including patient and consumer groups; and
- a comment period to provide feedback regarding the LA/SA IAS posted on the website.

Based on comments received during the consultation period, the document *Look-alike Sound-alike Health Product Names: Comments and Responses to the Issue as presented in the Issue Analysis Summary* was developed in order to respond to stakeholders comments/questions.

Furthermore, based on stakeholder feedback, this IAS has been revised and suggestions will be considered and incorporated when developing the draft guidance document.

Consultation activities are planned for the future when policy is further developed. Details, such as the sponsor submission requirements and implementation details etc., will be developed and proposed as we move forward in policy development.

8. NEXT STEPS

It is anticipated that HPFB will move forward in implementing pre and post-market recommendations. In the Spring/Summer of 2004, it is intended that a draft policy document will be developed for prescription drugs, followed shortly thereafter with a consultation period where stakeholder comments will be considered. During this time, HPFB will be attempting to acquire a computer application that will screen for possible LA/SA health product names.

Appendices

APPENDIX A

January, 2003

updated July 2003, February 2004

DRAFT

FDA and its response to look-alike sound-alike proprietary product names

Over the past decade, the FDA has attempted to minimize medication errors attributed to look-alike sound alike drug names. The FDA considers the review of a proprietary name to be an important part of the review of any new application[19]. FDA officials have stated that the "FDA must do everything within its authority to maximize the likelihood that approved products will be used correctly in the real world" (Peter Honig, M.D.) and "FDA's goal is to try and catch the potential for error before the product is marketed"(Sharon Smith Holston, FDA's Deputy Commissionaire for External Affairs).

Within the FDA, the Center for Biologics Evaluation and Research (CBER) and the Center for Drug Evaluation and Research (CDER) have the responsibility for helping ensure the safe and effective use of the drugs they approve by identifying and avoiding proprietary names that contribute to problems in the prescribing, dispensing, or administration of a product. Because early identification of a potentially confusing proprietary name is crucial, CBER and CDER review these proposed names prior to approval of a new drug application.

The Regulations

The Food Drug and Cosmetic Act (Act) - section 502(a) states that a drug is misbranded "if its labeling is false or misleading in any particular." The implementing regulations for this section of the Act, reference 21 CFR 201.10(C)(1) through (5), lists five factors that could make the labeling for a drug misleading[20]. They are:

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[19]Dr. J Jenkins, Director of the Office of New Drugs, CDER, "Proprietary Names and the Drug Approval Process". *Proc. of Evaluating Drug Names for Similarities: Methods and Approaches Public Meeting.* Washington D.C. , June 26, 2003.

[20]"Review of CBER Regulated Product Proprietary Names. Appendix 2: Criteria for Review of Biological Product Proprietary Names."*Manual of Standard Operating Procedures and Policies, General Information Review. SOPP8001.4 Version #1,* August 15, 2002.U.S. Food and Drug Administration, Center for Biologics Research and Evaluation. <http://www.fda.gov/cber/regsopp/80014app2.htm>.

1. The order in which the names of the ingredients present in the drug appear in the labeling, or the relative prominence otherwise given such names.

2. Failure to reveal the proportion of, or other fact with respect to, an ingredient present in such drug, when such proportion of other fact is material in the light of the representation that such ingredient is present in such drug.

3. **The employment of a fanciful proprietary name for a drug or ingredient in such a manner as to imply that the drug or ingredient has some unique effectiveness or composition when, in fact, the drug or ingredient is a common substance, the limitations of which are readily recognized when the drug or ingredient is listed by its established name.**

4. The featuring in the labeling of inert or inactive ingredients in a manner that creates an impression of value greater than their true functional role in the formulation.

5. **Designation of a drug or ingredient by a proprietary name that, because of similarity in spelling or pronunciation, may be confused with the proprietary name or the established name of a different drug or ingredient.**

At the FDA, 21 CFR 201.10(c)(5) is the basis for the safety review of LA/SA drug names.

Pre-Market Review

Look-alike (orthographic) sound-alike (phonetic) proprietary names are reviewed by the Advertizing and Promotional Labeling Branch (APLB) within CBER and by the Division of Medication Errors and Technical Support (DMETS) within the Office of Drug Safety (ODS) [formerly known as the Office of Post-marketing Drug Risk Assessment (OPDRA)] within CDER.[21]

The authority to review look-alike sound-alike drugs is based primarily on factor five and

[21]T. G. Phillips, "DMETS Evaluation of Proprietary Names", *Proc. of Evaluating Drug Names for Similarities: Methods and Approaches Public Meeting.* Washington D.C. , June 26, 2003.

to a lesser extent on factor three[22] of the regulations listed above. In determining whether the degree of similarity in spelling or sound of names may be problematic, the following potential contributing factors are taken into consideration during review:

- the dosage forms or routes of administration,
- the marketing status (Rx or OTC),
- the indication(s) and directions for use,
- the storage configuration,
- the clinical setting for dispensing or use (inpatient or outpatient hospital or clinic vs. retail pharmacy for use at home),
- the packaging and labeling, and
- the strength.

Generally, if one or more of these factors are different enough that the potential for confusion can be minimized, there may be less concern with the name since the chance of a medication error is smaller.

Apart from look-alike sound-alike names, there are other naming factors that appear to increase the possibility of medication errors[23]. They include the following:

- Different proprietary names for the same active ingredient

  Products with different proprietary names for the same active ingredient are avoided because safety concerns may arise if

  (a) products with two different proprietary names but the same active are concomitantly prescribed, or

  (b) a patient is allergic to an active ingredient but unknowingly takes it because the product has a different proprietary name.

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[22]"Review of CBER Regulated Product Proprietary Names. Appendix 2: Criteria for Review of Biological Product Proprietary Names."*Manual of Standard Operating Procedures and Policies, General Information Review*. *SOPP8001.4 Version #1*, August 15, 2002.U.S. Food and Drug Administration, Center for Biologics Research and Evaluation. <http://www.fda.gov/cber/regsopp/80014app2.htm>.

[23]Dr. J Jenkins, Director of the Office of New Drugs, CDER, "Proprietary Names and the Drug Approval Process". *Proc. of Evaluating Drug Names for Similarities: Methods and Approaches Public Meeting.* Washington D.C. , June 26, 2003.

- Product line extensions

  Using the same name for a drug containing none of the same actives as the original would likely not be approved because it has the potential for confusion.

- USAN names in proprietary names

  The use of USAN stems in proprietary names is avoided because it may create confusion in differentiating a drug's proprietary name from a common or established name. In addition, such use has the potential to limit selection of new USAN names.

Both APLB and DMETS make recommendations to the appropriate review divisions that make the final decision regarding any look-alike sound-alike issue.

Although CBER and CDER have independent processes regarding the review of potential look-alike sound-alike drugs, when contentious issues arise, the Office of Drug Safety (ODS) within CDER is consulted.

Since October 1999, ODS (formerly OPDRA) has reviewed approximately 400 proposed proprietary names for drug products. Proprietary names undergo a multifactoral review designed to improve consistency and minimize risk with sound-alike and look-alike names. [24]

The review of proprietary names can begin as early as the end of Phase II of an IND or as late as when an NDA/ANDA is filed. At this time, FDA feedback is preliminary in nature because it is possible that another product may be approved, prior to the proposed product in question, that could result in unforseen LA/SA confusion. As a result, a final abbreviated review of the proposed proprietary name is completed within 90 days of the anticipated day of approval that focuses specifically on trade names that were approved by the FDA from the time of first review until approval of the NDA.[25]

The name review process includes the following:[26]

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[24]C. Holquist, T.G. Phillips, "FDA Safety Page: How FDA reviews drug names." *Drug Topics*, April 2, 2001.<http://www.fda.gov/cder/drug/MedErrors/reviewDrugNames.pdf>

[25]T. G. Phillips, "DMETS Evaluation of Proprietary Names." *Proc. of Evaluating Drug Names for Similarities: Methods and Approaches Public Meeting.* Washington D.C. , June 26, 2003.

[26]C. Holquist, T.G. Phillips, "FDA Safety Page: How FDA reviews drug names." *Drug Topics*, April 2, 2001.<http://www.fda.gov/cder/drug/MedErrors/reviewDrugNames.pdf>

An Expert panel review: The primary focus of the expert panel is to identify potential sound-alike, look-alike names. This panel meets weekly to exchange opinions on the safety of new proprietary names. Within CDER, the panel consists of approximately 10 clinical pharmacists from DMETS within ODS staff and representatives from the Division of Drug Marketing and Advertizing Communications (DDMAC). The pharmacists use their clinical, regulatory and professional experience to decide on the acceptability of a proprietary name while DDMAC representatives comment on the promotional aspects of the name. Often, an extensive review of a number of drug reference texts and FDA internal databases is performed. In addition, the panel looks for factors of look-alike, sound-alike products that may contribute to errors such as overlapping strengths and similarities in dosing regimens. Each member provides a written copy of their recommendation and minutes are recorded. Within CBER, it appears that a similar expert panel exists.

Handwriting and Verbal Analyses: Handwriting and verbal analyses are conducted within the FDA to determine the degree of confusion in visual appearance or pronunciation between the proposed proprietary name and the names of other U.S. drugs. In an attempt to simulate the prescription ordering process, FDA health professionals (130 volunteer nurses, pharmacists and physicians) are required to interpret both written inpatient and outpatient prescriptions and verbal orders. They provide written interpretation of a name via e-mail and comments on related products that could increase chance of error.

Computer-assisted analysis: ODS and APLB are using a newly acquired computer application, Phonetic and Orthographic Computer Analysis (POCA), to evaluate drug names for LA/SA similarities. POCA uses phonetic and orthographic algorithms to provide a percentage ranking of similarity between the proposed name and the databases of existing proprietary names. Furthermore, POCA also considers similar strengths and dosage forms when looking at a name to identify potential sound-alike and/or look-alike proprietary names[27].

Labeling and packaging analysis: ODS and APLB provide a safety assessment of the container labels, carton and package insert labeling, and proposed packaging of each product to identify areas for potential improvement.

Overall Risk Evaluation: This final phase of the name review weighs the results of each phase of the review in an overall risk-benefit analysis. Additional risk factors or mitigating factors, such as intended population, overlapping strengths, dosage forms, dosing recommendations, indications for use, storage, labeling, packaging and lessons learned from post-marketing experience (risk benefit analysis) are also considered.

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[27]T. G. Phillips, "DMETS Evaluation of Proprietary Names", *Proc. of Evaluating Drug Names for Similarities: Methods and Approaches Public Meeting.* Washington D.C. , June 26, 2003.

Additional resources that are used to examine look-alike sound-alike drugs include the Adverse Event Reporting System (AERS) Drug Quality Reporting System (DQRS), National Library of Medicines MEDLINE database, clinical and regulatory experience and literature reports.

In accordance with the FDA's recent concept paper "Premarketing Risk Assessment", ODS and ADLS are encouraging sponsors to submit a risk assessment and evaluation to support the safety of a proprietary trade name. This suggestion has been advocated by the Institute of Medicine in its December 1999 report "to Err is Human" and recommended by the Health and Human Services Advisory Committee on Regulatory Reform (November, 2002).

In addition, the FDA suggests to sponsors that they routinely submit a back-up trade name.

Post Marketing:

ODS and ADLS monitor all postmarketing reports of medication errors that are related to naming, labeling and packaging of drug products. Each report is classified for severity, type and cause of error. If appropriate, ODS or ADLS make specific recommendations to the appropriate reviewing divisions regarding changing the labeling packaging or proprietary name. If appropriate, the FDA will work with the manufacturer to correct the problem by making a change in the packaging, labeling or name. For instance, the FDA recently issued 142 letters to sponsors ordering label changes to highlight confusing names[28]. Similar names, for example, will be labeled as "ChlorproMAZINE" and "ChloproPAMIDE" and special shading and different-coloured letters will also help distinguish look-alike drug names.

CDER and CBER provide feedback to health care professionals regarding medication errors through publications in the FDA's Medical Bulletin, the FDA Consumer Magazine and collaborates with USP and AMA's Institute for Safe Medication Practices.

Future plans/projects:

The Division of Medical Errors and Technical Support within ODS is working on a proposal that will require bar coding on all prescription medications[29]. Initially, bar-coding would be used in an inpatient basis but will eventually be applied to increase the

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[28]Lauran Neergaard, "FDA Pushes to Curb Drug Mix-ups", *The Boston Globe*, February 1, 2002

[29]Mary Gross, Office of Drug Safety, CDER, Bar Coding Human Drugs and Biologics-A Regulatory Initiative.Proc from the 38th Annual Drug Information Association Meeting, Chicago, Illinois, June 16-20, <http://www.fda.gov/cder/present/DIA62002/gross/sld001.htm>

accuracy of dispensing on an outpatient basis. Ultimately, physicians will be able to generate computerized prescriptions containing barcodes that, when received by a pharmacist, can be recorded electronically. The pharmacist would then select the desired product from the shelf and scan the barcode of the product which would be linked to the electronic record of the prescription order.

ODS plans to modify its Adverse Event Reporting System (AERS) by incorporating a Taxonomy of Medical Errors to enhance its ability to detect medication errors, including look-alike sound-alike medication errors. This taxonomy will allow the staff to perform trend analysis based upon the numerous causes and types of medical errors, which is currently not available through AERS.[30]

Currently, the division is also working on four documents for industry that include[31]:

1. a policy and procedures manual with the purpose of minimizing medical errors[32],
2. a guidance document on the FDA process for submitting proprietary names for evaluation,
3. a guidance document outlining how to safely label and package drugs, and
4. a guidance document outlining Industry's role in evaluating a new proprietary drug name[33].

The first two of these documents will be posted on the CDER website in the near future.

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[30]Office of Drug Safety Annual Report 2001, Center for Drug Evaluation and Research, Food and Drug Administration. <http://www.fda.gov/cder/Offices/ODS/AnnRep2001/annualreport2001.htm>

[31]Guidance Agenda: Guidances CDER is Planning to Develop During FiscalYear 2003http://www.fda.gov/cder/guidance/guidance-agenda.htm

[32]P.E. Clarke, "Resources to track and reduce medication errors increased", CDER News along the Pike, Vol. 8, Issue 2, July 24, 2002. <http://www.fda.gov/cder/pike/janfeb2002.pdf>

[33]T. G. Phillips, "DMETS Evaluation of Proprietary Names", *Proc. of Evaluating Drug Names for Similarities: Methods and Approaches Public Meeting.* Washington D.C. , June 26, 2003.

APPENDIX B

Look-alike Sound-alike Options (pre and post-market)

Policy Related Options (Pre-market)

General Options

Option 1: Status Quo: Case by case approach

Description:

LA/SA health product name similarities would continue to be reviewed on a case by case basis without any consistent or formal process in place. The review would continue to be arbitrary and depend on initiative, memory, intuition and judgement of staff. When a proposed LA/SA product name is identified, the sponsor would be notified and encouraged but not forced to consider changing their product name.

Pros	Cons
▸ minimal resources	▸ cause of morbidity and mortality
▸ no additional regulatory burden	▸ liability
▸ short term thinking	▸ reactive
▸ stakeholders may take lead in developing a solution	▸ no strategy
▸ more cases/precedents that may allow criteria to be developed for future policy etc.	▸ abrogating our responsibility
▸ some stakeholders will appreciate status quo	▸ not being consistent
	▸ other regulatory bodies are doing something
	▸ low tech
	▸ reinvent wheel through case by case evaluation
	▸ lack of respect from stakeholders

Analysis:

Without a specific process in place and mixed results regarding the initial identification and subsequent action to resolve safety concerns regarding LA/SA health product names, a number of real and potential risks would continue to exist including:

- the morbidity and mortality of Canadians due to medication errors,
- the risk that public trust may be lost and the public perception may be that HPFB

cannot adequately prevent the harm of Canadians; and

- liability as a result of inconsistent decisions and/or liability for failure to meet responsibilities outlined in the HPFB mandate if Canadians suffer morbidity and mortality due to medication errors.

Policy Related Options

Option 2: Policy/Guideline /SOP

Description:

A policy, guideline and/or SOP would be developed specifically to address LA/SA health product name issues.

Pros	Cons
▸ rationalizes and explains expectations and principles ▸ responsibilities are known ▸ resource requirements can be estimated in the long term ▸ don't need to change regs (as per legal opinion) ▸ consistent dealing with industry (fairness) ▸ proactive, objective, long term strategy ▸ all interested parties can comment (allows for wide airing) ▸ reduced liability ▸ consistent with First Ministers Meetings and Health Accord ▸ limit number of LA/SA health product name issues post-market ▸ reduce compliance issues ▸ should contribute to safety ▸ positive press	▸ short term resources ▸ compliance and enforcement ($)-long term ▸ low tech ▸ public involvement -$ ▸ negative press (raises profile)

Analysis:

When policy is properly developed and consistently applied, it should result in a fair, systematic and consistent method of assessing LA/SA health products names. However, it has been acknowledged that any policy would need to be complimented with, at

minimum, a computer application and some formal review process.

Option 3: Regulation/Legislation

Description:

Legislation and/or regulations would be developed specifically to address LA/SA health product name issues to clarify actions that could be taken by HBFB respecting LA/SA names (i.e. Regulations similar to the U.S.).

Pros	Cons
▸ could be tied to legislative renewal ▸ regulatory changes would clarify actions that could be taken by HPFB respecting LA/SA names ▸ one could leverage policy with regulations ▸ signals importance of issue ▸ compliance and enforcement: clear guidelines and parameters ▸ proactive, objective, long term	▸ time and $ ▸ current legislation is inflexible ▸ unnecessary ▸ alternative methods of achieving same goal ▸ Regulatory Policy- last resort, must show that it is the only option (avoid if possible) ▸ liability issues with compliance ▸ low tech ▸ difficult to change ▸ long term

Analysis:

The Cabinet Directive on Law Making[34] states that law should only be used when it is most appropriate and there are no other ways to achieve policy objectives effectively. The Federal Regulatory Policy[35] makes a similar statement regarding regulation making (i.e government will weigh the benefits of alternatives to regulation, and of alternative regulations, against their cost, and focus resources where they do the most good).

Furthermore, the LA/SA WG believes that the *Food and Drug Regulations* provides

[34]"The Cabinet Directive on Law Making", Government of Canada Privy Council Office, March 1999.<http://www.pco-bcp.gc.ca/default.asp?Page=Publications&Language=E&doc=legislation/lmgcabinetdirective_e.htm>

[35]"Government of Canada Regulatory Policy", Government of Canada Privy Council Office, November1999.<http://www.pco-bcp.gc.ca/raoics-srdc/docs/publications/regulatory_policy_e.pdf>

authority to impose a pre-market requirement that the drugs not be confusing with one another [see subsections.C.08.002.(1), C.08.002.(2), C.08.002.(3) and C.01.014.1(2) of the *Food and Drug Regulations*]. If a sponsor does not comply with these sections, HPFB need not issue a DIN (new drugs and drugs other than new drugs) and/or NOC (new drugs only), as applicable.

Following issuance of an NOC and/or DIN for a drug, the LA/SA WG is of the opinion that HPFB can use C.01.013. of the *Food and Drug Regulations* to require the manufacturer to establish the safety of the drug under its recommended upon becoming aware of a safety or efficacy concern associated with LA/SA name confusion. If sufficient evidence is not provided, sales of the drug can be suspended.

Computer Related Options

The sheer number of existing medication names makes it unlikely that manual evaluation of the potential for confusion between names would ever be comprehensive enough to be viewed as reliable.[36]

Option 4: Use of current Drug Submission Tracking System (DSTS)

Description:

The Drug Submission Tracking System is an internal system that has been in use since 1994. It records and tracks drug submission information. The existing computer application would be used to detect similarities in spelling among health product names.

Pros	Cons
▸ DSTS system currently in place for drugs for human use ▸ time saver/saves review time ▸ low cost ▸ consistent, proactive, long term, objective, systematic ▸ can be used pre and post-market ▸ "wild card" can be used to search for	▸ DSTS system only in place for drugs for human use (not vet drugs, medical devices etc...) ▸ DSTS can only detect similarities in spelling (not sounds) ▸ history from 1994 only (no products filed prior to this are included in the DSTS system) ▸ DSTS system has its challenges (dated, slow, difficult to print from)

[36]B. L. Lambert., "Predicting look-alike and sound-alike medication errors", *Am. J. Health-Syst Pharm.* May 1997 (54):1161-1171.

similarities in names ▸ appears similar to a process that is being used by the TGA (Australia).	▸ system should be expanded to have the capacity to flag same/similar names ▸ challenges associated with adding extra functions to DSTS ["any" changes to DSTS require hiring an external consultant (no internal expertise)] ▸ validation required ▸ an SOP would be required to ensure a systematic search ▸ needs to be complemented by human element (i.e. expert evaluation of error potential) ▸ manual intensive process ▸ human resources required ▸ DSTS not intended to be used to detect LA/SA health product name similarities

Analysis:

The DSTS system is currently in place for drugs for human use. Through its "wild card" feature, it is able to do a crude search of LASA health product names. However, those who are most familiar with the system believe that DSTS is not equipped to identify LA/SA health product names. In addition to the problems listed above, it would likely detect too many potential LA/SA health product name similarities.

Option 5: Use of Current Records System (iRIMS™)

Description:

The integrated Records Information Management System (iRIMS™) is an internal computer application used as a filing system by a Central Registry who houses files for the Branch. The existing IRIMS computer application, that is used in the Central Registry, would be used to detect similarities in spelling among health product names.

Pros	**Cons**
▸ iRIMS™ system currently in place ▸ used by all Directorates in HPFB ▸ history (previous ARMS system was incorporated into iRIMS™)	▸ iRIMS™ system search capabilities are limited to information that is provided when the CR file is created (brand name or generic name) ▸ Company files exist prior to 1990 (not stored by generic or brand name)

▸ time saver/saves review time ▸ low cost ▸ consistent, proactive, long term, objective, systematic ▸ can be used pre and post-market ▸ "wild card" can be used to search database	▸ iRIMS™ can only detect similarities in spelling (not sounds) ▸ system should be expanded to have the capacity to flag same/similar names ▸ challenges associated with adding extra functions to iRIMS™ ("any" changes to iRIMS™ requires consultation with the iRIMS™ owners); ▸ Central Registry (CR) not currently involved in submission processing (permission would be required to get access) ▸ an SOP would be required to ensure a systematic search ▸ needs to be complemented by human element (i.e. expert evaluation of error potential) ▸ manual intensive process ▸ human resources required ▸ iRIMS™ not intended to be used to detect LA/SA health product name similarities ▸ the iRIMS™ administrator does not support this option

Analysis:

The iRIMS™ system is currently used by all directorates within HPFB, however, its search capabilities are limited to the information that is provided when the CR file is created. In summary, a name could be listed by just the brand name, just the trade name or both. As it currently exists, this system will not necessarily be able to detect name similarities because they may not be input into the system in the first place.

Option 6: Build an internal system to detect LA/SA health product name similarities

Description:

A computer application would be developed in-house to detect similarities in the spelling and sounds among health product names.

Pros	**Cons**
▸ could be built in house using Branch staff ▸ could be used by all Directorates in HPFB ▸ time saver/saves review time ▸ low cost ▸ consistent, proactive, long term, objective,	▸ system needs to be built ▸ cannot use a Lotus notes application ▸ system will likely only detect similarities in spelling (not sounds) ▸ data input required

systematic ▸ can be used pre and post-market ▸ "wild card" can be used to search database ▸ recommended by iRIMS™ administrator ▸ system could be expanded to have the capacity to flag same/similar names	▸ an SOP would be required to ensure a systematic search ▸ needs to be complemented by human element (i.e. expert evaluation of error potential) ▸ manual intensive process ▸ human resources required

Analysis:

The feasibility of this option is currently being considered further by a Branch computer development team (Céline Talbot, Project Manager, Lotus Notes Applications, Office of Management Services, Health Canada). The main obstacle to this option is that a system would need to be built and would likely only detect similarities in spelling (not sounds).

Option 7: Basic Computer application

Description:

A computer application would be acquired to detect similarities in the spelling and sounds among health product names.

Pros	**Cons**
▸ may be suitable off-the-shelf program available ▸ time saver/saves review time ▸ high tech ▸ have data available in DSTS/DPD to input into system ▸ cost recovery - potential of sharing software with industry ▸ consistent, proactive, long term, objective, systematic ▸ can be used pre and post-market ▸ Ottawa - good location for programmers ▸ consistent approach (objective, reliable)	▸ resources to program computer ▸ need to input data - labour intensive ▸ not infallible (false positives and false negatives) ▸ validation required ▸ needs to be complemented by human element (i.e. expert evaluation of error potential) ▸ resources, $ ▸ training required

Analysis:

A computer application similar to that used currently by the FDA is possibly a feasible option that could screen for LA/SA health product names. When a LA/SA health product name is identified by the application, the reviewer/review committee could consider it

further. It is anticipated that resources would be required to tailor the system to meet HC needs.

Option 8: LA/SA-specific computer application with added features

Description:

A computer application with an ability to uncover potential problems arising from LA/SA health product names and their contributing factors (similar dosage and strengths) is an option Health Canada (HC) could use to screen for LA/SA health product names. Furthermore, this application also has the ability to identify other nomenclature problems, such as confusion with medical terminology, jargon, abbreviations etc.

Pros	Cons
▸ may be suitable off-the-shelf program available ▸ time saver/saves review time ▸ high tech ▸ theoretically based ▸ have data available in DSTS/DPD to input into system ▸ cost recovery - potential of sharing software with industry ▸ consistent, proactive, long term, objective, systematic ▸ can be used pre and post-market ▸ Ottawa - good location for programmers	▸ resources to program computer ▸ need to input data - labour intensive ▸ not infallible (false positives and false negatives) ▸ needs to be complemented by human element (i.e. expert evaluation of error potential) ▸ resources- $ ▸ specialized skill set -contractors programmers ▸ potentially too sensitive (validation required) ▸ overkill? ▸ training requirements ▸ may not be necessary if other processes in place ▸ - onus on management ▸ large volume health product names

Analysis:

A LA/SA specific computer application has most of the same benefits and drawbacks as the previous option but it is likely more “astute” at finding LA/SA similarities between health products. Cost to acquire the application may be a potential barrier to this option.

Review Process Options

Option 9: Foreign Review (FDA)

Description:

Proposed health product names would be reviewed by the U.S. using their current system to review names (see "FDA and its response to look-alike sound-alike proprietary product names" in Section 5.2: International Perspective).

Pro	Cons
▸ existing process at FDA ▸ FDA has experience and expertise in name review ▸ minimal additional HC human resources required ▸ HC has confidentiality agreement with U.S. ▸ no change in regulations required ▸ long term, proactive	▸ FDA not likely to be willing to provide service ▸ dependent on FDA workload (FDA backlog issues) ▸ low priority for FDA ▸ dependent on FDA/lack of control ▸ FDA is currently reviewing drug names and not health product names ▸ different drug names sometimes used in the U.S. (sometimes drugs may not be filed in U.S. or filed in Canada first) ▸ proprietary issues ▸ may be expensive ▸ may complicate cost recovery ▸ lack of internal expertise ▸ liability issues - HC has ultimate responsibility ▸ internal resistance to foreign drug reviews - not a Canadian made solution ▸ may be difficult to overrule U.S. decisions

Analysis:

The FDA currently reviews only drug names (for human use) and not all health products. To date, their process is superior to any other regulatory agency, however, the FDA will not likely be willing to provide the service and, if provided, HC would be dependent on the FDA (re timelines, expertise etc...). Furthermore, HC is ultimately responsible for any decision it makes. As a result, this option has its limitations.

Option 10: Review by Third Party

Description:

Proposed health product names would be reviewed by a third party. The sponsor would provide a certification to HC that states that the name is acceptable w.r.t. LA/SA health

product name similarities.

Pros	Cons
▸ Pharmaceutical Advertising Advisory Board (PAAB), a third party, currently reviews advertising related to drugs ▸ third party expertise with experience in name review in the U.S. ▸ Canadian expertise in name review would develop if there was a need ▸ no backlog issue-review would be complete prior to sponsor filing submission ▸ minimal additional HC human resources required ▸ low cost to HC ▸ long term, proactive	▸ Food and Drugs Act and Regulations does not require pre-authorization of advertising material ▸ no Canadian third party currently exists with expertise and experience in the review of health product names ▸ dependent on third party for review decision (lack of control w.r.t. final decision), ▸ liability issues - HC has ultimate responsibility (C.08.002-a safety issue) ▸ change in regulations required? ▸ lack of internal expertise would result ▸ proprietary issues ▸ additional cost to sponsor

Analysis:

This option has all the same concerns of the previous option (foreign review). Furthermore, no Canadian third party has the expertise or experience to review health product names.

Option 11: Name review (internal)

Description:

Proposed health product names would be reviewed by the appropriate staff in HPFB.

Pros	Cons
▸ proactive, long term, no change in regulations required ▸ will establish internal expertise ▸ flexibility to change rules/screening criteria ▸ documentation on CR file	▸ human limitations to detect LA/SA health product names (i.e. the sheer number of health product names) ▸ need for assistance from computer for LA/SA health product name detection ▸ subjective/one person's opinion ▸ no formal interdirectorate collaboration ▸ different skill set required (from traditional review) ▸ human resources and training required

	▸ potential increase in time to review (and NOC) ▸ policies and guidelines required ▸ difficult to retrace steps to relevant CR file when a similar issue arises with another product

Analysis:

Due to the sheer number of possible health product names, a name review would have to be complemented with a computer application that would initially screen the product for LA/SA name similarities to other health products. This option is a possibility, assuming resources and training can be made available.

Option 12: Name review committee (similar to Therapeutic Product Classification Committee (TPCC))

Description:

Proposed health product names would be reviewed by an inter-directorate committee.

Pros	Cons
▸ collaboration between directorates ▸ decisions recorded ▸ consistency ▸ decisions made across product lines (i.e. human prescription drugs/vet. drugs) ▸ sponsor more readily accepts decision from a committee ▸ 1st level of appeal process could be incorporated into the committee (as per TPCC) ▸ no change in regulations, long term, proactive ▸ reduced liability	▸ decisions may not occur on a timely basis (dependent on committee's meeting times) ▸ human limitations to detect LA/SA (i.e. the sheer number of health product names) ▸ need for assistance from computer (LA/SA detection) ▸ can only look at a limited number of LA/SA issues (may still need reviewer to do some work or computer application for an initial screen)

Analysis:

As with the previous option, a name review committee would have to be complimented with a computer application. This option is a possibility but it must be realized that decisions via committees, even though less subjective than a name review, may not occur on a timely basis and the committee could only look at a limited number of LA/SA issues.

Sponsor filing requirement options

Option 13: Sponsor provides a list of name choices

Description:

The sponsor provides a list of product name choices for each submission, in order of preference.

Pros	Cons
▸ communicates to sponsor LA/SA potential ▸ second name review could be external to review ▸ may save sponsor time ▸ no change in regulations required	▸ not a stand-alone process ▸ optional ▸ potential for confusion- internal tracking system needs to keep up with the name change ▸ potential for delays if 1st name rejected (stop the clock mechanism?)

Analysis:

This option would need to be considered as a complement to any recommendation.

Option 14: Sponsor does LA/SA search and analysis

Description:

The sponsor does a complete name search and analysis that is provided with the submission to ensure that the proposed product name does not have LA/SA similarities to other health products.

Pros	Cons
▸ sponsor assumes more responsibility (by considering LA/SA similarities up front) ▸ fewer HC resources required than if complete LA/SA analysis done in-house ▸ may create business opportunities (Industry may contract out work) ▸ reduces name review time (if submission is complete) ▸ long term, proactive, no change in regulations required	▸ not a stand alone process ▸ HC must set criteria for industry ▸ HC monitoring and enforcement required ▸ skill set- no Canadian companies are involved in LA/SA search- sponsors may need to contract out to American companies ▸ more Industry resources required, increased burden ▸ potential resistance from sponsor ▸ policy, guidelines required

	▸ computer application required?

Analysis:

This option, which would have to be a compliment to the final recommendation, requires that the sponsor assumes more responsibility by considering the potential for LA/SA health product name similarities before filing.

Option 15: Require trademarks

Description:

The sponsor is required to obtain a registered trade-mark for a proposed health product name.

Pros	Cons
▸ sponsor will be required to have a Trade-mark ▸ Trade-mark computer system/application exists ▸ fewer HC resources required ▸ long term, proactive	▸ Industry Canada is not as concerned about LA/SA health product names if the same sponsor has products with similar names ▸ time required to obtain a trade-mark is approximately 2 years ▸ dependent on Industry Canada ▸ Industry Canada would not carry out or be concerned about a risk benefit analysis (i.e. concomitant strengths, dosage) ▸ Industry Canada has a different focus than HC (concerned about protecting commercial interests of firms holding existing trademarks and not concerned with safety) ▸ increased workload for Industry Canada ▸ Industry Canada buy in required ▸ if mandatory - change in regulations required ▸ sponsors have increased regulatory burden ▸ still need internal expertise ▸ what about older products? ▸ data entry of product name and generic name required ▸ HC monitoring and enforcement required

Analysis:

Requiring trade-marks for all health products, if mandatary, would require a change to the regulations. Furthermore, this would result in an increased workload for Industry Canada and sponsors would have an increased regulatory burden (it takes approximately 2 years to obtain a trade-mark).

There is some question that all LA/SA health product names issues could be resolved with this option as Industry Canada is not as concerned about LA/SA health product names if the same sponsor has products with similar names.

Other

Option 16: Combination of options

Description:

The recommended pre-market option could involve any permutation and combination of the 15 options mentioned above.

Analysis:

The LA/SA WG agrees that the final pre-market recommendations will have to have contain a combination of options [i.e., policy element/computer element/human (reasoning) element].

Policy Related Options (Post-market)

General

Option 1: Status Quo

Description:

LA/SA health product name similarities would continue to be discovered on an ad hoc basis (it would depend on the initiative of staff) without any consistent or formal process in place. When a LA/SA health product name is identified post-market, the sponsor would be notified and encouraged to consider changing their product name.

Pros	Cons
▸ minimal resources	▸ cause of morbidity and liability for people

▸ no additional regulatory burden	▸ reactive
▸ short term thinking ▸ manufacturers' responsibility ▸ stakeholders may take lead in developing a solution ▸ more cases/precedents that may allow criteria to be developed for future policy etc. ▸ some stakeholders will appreciate	▸ no strategy ▸ abrogates our responsibility ▸ not being consistent ▸ other regulatory bodies are doing something ▸ low tech ▸ reinvent wheel by case-by-case evaluation ▸ lack of respect from stakeholders

Analysis:

Without a specific process in place, and mixed results regarding the identification and subsequent action to resolve safety concerns regarding LA/SA health product names, a number of real and potential risks exist including:

- the morbidity and mortality of Canadians due to medication errors,
- the risk that public trust may be lost and the public perception may be that HPFB cannot adequately prevent the harm of Canadians; and
- liability as a result of inconsistent decisions and/or liability for failure to meet responsibilities outlined in the HPFB mandate if Canadians suffer morbidity and mortality due to medication errors.

Policy Related Options

Option 2: Policy/Guideline /SOP

Description:

A policy, guideline and/or SOP would be developed specifically to address LA/SA health product name issues.

Pros	**Cons**
▸ rationalizes and explains expectations and principles ▸ responsibilities are known ▸ resource requirements can be estimated in the long term ▸ don't need to change regs (as per legal opinion) ▸ consistent dealing with industry (fairness)	▸ short term resources ▸ compliance and enforcement ($) - long term ▸ low tech ▸ public involvement - $ ▸ negative press (raises profile) ▸ grandfathering

▸ proactive, objective, long term strategy ▸ all interested parties can comment (allows for wide airing) ▸ public involvement with stakeholders ▸ reduced liability ▸ consistent with First Ministers Meetings and Health Accord ▸ limit #'s of issues post-market ▸ reduce compliance issues ▸ should contribute to safety ▸ positive press	

Analysis:

When policy is properly developed and consistently applied, it should result in a fair, systematic and consistent method of addressing LA/SA health products names. However, it has been acknowledged that any policy would need to be complimented with one of the post-market options listed below.

Option 3: Legislation/Regulations

Description:

Legislation and/or regulations would be developed specifically to address LA/SA health product name issues to clarify actions that could be taken by HPDF respecting LA/SA names (i.e. Regulations similar to the U.S.).

Pros	**Cons**
▸ could be tied to legislative renewal ▸ regulatory changes would clarify actions that could be taken by HPFB respecting LA/SA names ▸ one could leverage policy with regulations ▸ signals importance of issue ▸ compliance and enforcement: clear guidelines and parameters ▸ proactive, objective, long term	▸ time and $ ▸ legislation inflexible ▸ unnecessary ▸ reduces alternative methods of achieving same goal ▸ Regulatory Policy - last resort, must show that it is the only option (avoid if at all possible) ▸ liability issues with compliance ▸ low tech ▸ difficult to change ▸ long term ▸ less industry cooperation in the dev't of

	regulations (re: public involvement)

Analysis:

The Cabinet Directive on Law Making (1999) states that other options should be considered before law making. The Federal Regulatory Policy (1999) makes a similar statement regarding regulation making.

Furthermore, legal opinion has already shown that the *Food and Drug Regulations* is useful in providing authority to impose a pre-market and post-market requirement that the names of drugs not be confused with one another. Pre-market, if a sponsor refuses to comply, HPFB need not issue a DIN (new drugs and drugs other than new drugs) and/or NOC (new drugs only), as applicable. Post-market, sales of a drug can be suspended when sufficient evidence is not submitted to establish the safety of a drug under the conditions of use for which the drug is recommended.

<u>Computer Related</u>

Option 4: Barcoding

Description:

Barcoding of labels on health products would be used, possibly in conjunction with computerized prescriptions, in order to confirm that the right drug is being dispensed to the right patient.

Pros	**Cons**
▸ FDA currently considering barcoding ▸ applicable to hospital setting and pharmacy setting (Rx drugs) ▸ helps to reduce errors after Rx has been created ▸ proactive, long term	▸ jurisdiction ▸ outside of HC scope ▸ applicable to health products that are not prescribed? ▸ error happens upstream of barcoding - ▸ could not replace DIN ▸ not a stand-alone solution for the LA/SA health product names issue ▸ $ ▸ stakeholder investment required ▸ buy-in required by stakeholders ▸ stakeholder investment in bar code technology required

	▸ requires regulatory change if mandatory ▸ potential for system errors ▸ can we enforce

Analysis:

Of note, drug barcoding will soon be a legislated requirement in the U.S.

The WG believes that barcoding may be a good idea in the future. It cannot be a stand-alone solution, however, because errors can happen upstream from barcoding (i.e. when an Rx is written and misunderstood by the pharmacist). Furthermore, significant stakeholder investment would be required in barcoding. The Regulatory Policy specifically states that "information and administrative requirements are limited to what is absolutely necessary and imposes least possible cost."

Option 5: Electronic prescribing (printed scripts)

Description:

Prescriptions are prepared electronically.

Pros	**Cons**
▸ applicable for prescribed drugs only ▸ minimizes some LA/SA health product name errors (illegible handwriting on Rx)	▸ jurisdiction ▸ Provincial responsibility ▸ outside of HC scope ▸ not a stand-alone solution for the LA/SA health product name issue (many types of LA/SA errors can still occur) ▸ $ ▸ stakeholder investment required ▸ buy-in required by stakeholders ▸ potential for system errors ▸ can we enforce?

Analysis:

Similar to barcoding, electronic prescribing may be a good idea in the future but it cannot be implemented as a stand-alone solution because error can happen either upstream or downstream from the electronic prescription. Furthermore, significant stakeholder investment would be required in barcoding. The Regulatory Policy specifically states that when developing policy "information and administrative requirements are limited to what

is absolutely necessary and imposes least possible cost."

Sponsor Requirements

Option 6: Require the Sponsor to Change Name of the Health Product

Description:

HBFB would require a sponsor to change the name of their marketed health product once a LA/SA health product name issue is identified.

Pros	Cons
▸ legal authority exists if there is potential risk (refer to legal opinion) ▸ a potential mechanism to deal with grandfather issue ▸ long term, proactive	▸ resistance from stakeholders (re cost to stakeholders, brand recognition) ▸ recalls - potential for product shortage ▸ rebranding confusion ▸ post-market legal authority less strong than pre-market (enforcement is more difficult) ▸ no standardized regulatory authority/ methodology ▸ perceived bias against company ▸ usually 2 companies involved- who should change their name? ▸ legal appeals - proceedings ▸ reactive - resource intensive ▸ secondary screen to pre-market process

Analysis:

Requiring the sponsor to change the name of a product post-market would result in significant economic burden for sponsors (recalls, loss of brand recognition etc.). Benefits of requiring a sponsor to change the name of a product may not outweigh costs if one considers issues such as rebranding confusion and potential product shortages. The Regulatory Policy states that when developing policy,"adverse impacts on the capacity of the economy to generate wealth and employment are minimized and no unnecessary regulatory burden is imposed."

Option 7: Require Sponsor to Modify the Label of the Health Product

Description:

HBFB would require a sponsor to change the name of their marketed health product label once a LA/SA health product name issue arises, in order to differentiate the product from the one it is similar to.

Pros	Cons
▸ less $ to implement than name change ▸ specific solution to post-market products that have been on the market for a long time ▸ would not contradict labelling guidelines ▸ recall - product shortage can be mediated ▸ long term, proactive	▸ does not address spoken errors ▸ resistance from stakeholders (re cost to stakeholders) ▸ subjective ▸ perceived bias against company ▸ usually 2 companies involved- who should change their label? ▸ rebranding confusion ▸ policy change may be required

Analysis:

This option would be less harsh for sponsors that require the sponsor to change the name of the health product but it would still involve some economic outlays by the sponsor. This option would not be ideal and would be more of a compromise in that it would not address spoken errors.

Option 8 Monitoring

Description:

Use of various monitoring practices (i.e. ISMP, ADR reporting, Foreign reviews) to detect LA/SA health product name similarities post-market.

Pros	Cons
▸ proactive ▸ no change in regulations required ▸ long term solution ▸ may ensure consistency with other markets regarding LA/SA health product names ▸ may notice other issues (i.e. similar packaging) as a result of monitoring ▸ partnerships with stakeholders ▸ shared ownership of LA/SA monitoring (pre & post-market) ▸ have confidentiality agreements with	▸ not a stand alone solution (simply a way of identifying LA/SA health product name similarities) ▸ follow-up required ▸ compliance and enforcement of follow-up solution required ▸ increased workload ▸ resource intensive ▸ lack of linkages between databases

regulatory agencies ▸ could use pre-market system to look for LA/SA health product name similarities post-market ▸ a second screen	

Analysis:

This option would not be a stand alone solution and is simply a way of identifying LA/SA health product name similarities. Similarities would need to be promoted to reduce medication errors due to LA/SA health product name similarities.

Option 9 Health Promotion/Stakeholder Awareness

Description:

Increase awareness of documented LA/SA health product names to stakeholders by various means (e.g. info line, fact sheets, Dear Health Care Professional Letters, comments in ADR newsletter, LA/SA website, education about LA/SA health product names in medical schools)

Pros	Cons
▸ stakeholders could be involved ▸ prevention of preventable error ▸ FDA already working in this area ▸ proactive risk communication ▸ media involvement ▸ due diligence ▸ awareness/public involvement - may drive policy ▸ in some instances, existing mechanisms in place - tap into (e.g. Health Promotion Initiative)	▸ time intensive ▸ voluntary ▸ lack of control ▸ not all-encompassing ▸ difficult to measure effectiveness ▸ resources required ▸ media involvement (negative press)

Analysis:

For those products with LA/SA health product name similarities that are already on the market, promoting awareness of these similarities would likely reduce the incidence of medication errors due to LA/SA. This option is the least evasive and resource intensive for stakeholders involved.

Other

Option 10: Combination of options

Description:

The recommended post-market option could involve any permutation and combination of the 9 options mentioned above.

Analysis:

The LA/SA WG agrees that the final post-market recommendations are necessary and may contain a combination of options (i.e., policy element/promotion element).

Appendix C

Qualitative Exercise -Leading options to date

- Pick three of the twelve options. Rank from 1-3 (1 being the first choice, 2 being the second choice and 3 being the third choice)
- Put an asterisk beside the choice that could be implemented in the short term
- Put check mark (s) beside any complimentary or post market options

1. Policy & DSTS system & name review
2. Policy & DSTS system & name review committee
3. Policy & DSTS system & name review & name review committee

4. Policy & Build internal system & name review
5. Policy & Build internal system & name review committee
6. Policy & Build internal system & name review & name review committee

7. Policy & basic computer application & name review
8. Policy & basic computer application & name review committee
9. Policy & basic computer application & name review & name review committee

10. Policy & LA/SA specific computer application & name review
11. Policy & LA/SA specific computer application & name review committee
12. Policy & LA/SA specific computer application & name review & name review committee

Any of the above could be complimented with:

- check any below

1. Sponsor provides a prioritized list of name choices
2. Sponsor does search/analysis for LA/SA similarities

post-market options:

- check any below

1. Policy
2. Monitoring (environmental scan) & promotion
3. Promotion