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Stakeholders:

Subject: Look-alike Sound-alike (LA/SA) Health Product Names: Comments and Responses to the Issue as Presented in the Issue Analysis Summary

The purpose of this note is to inform you that following consultation with stakeholders regarding the LA/SA health product name issue and after a careful review of comments received, the LA/SA working group has developed responses to compiled comments. We thank all stakeholders for their constructive feedback and hope that this document responds to all issues raised. The attached document, *Look-alike Sound-alike Health Product Names- Comment and Responses to the Issue and Presented in the Issue Analysis Summary* 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:

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Thank you for your interest in this issue.

Original signed by

Julia Hill
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Enclosure

LOOK-ALIKE SOUND-ALIKE HEALTH PRODUCT NAMES COMMENTS AND RESPONSES TO THE ISSUE AS PRESENTED IN THE ISSUE ANALYSIS SUMMARY

Prepared by the LA/SA Working Group

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Health Products and Food Branch (HPFB)
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March 23 2004

LOOK-ALIKE SOUND-ALIKE HEALTH PRODUCT NAMES
COMMENTS AND RESPONSES TO THE ISSUE AS PRESENTED IN THE ISSUE ANALYSIS SUMMARY

1.0 WHY IS HEALTH CANADA INVOLVED IN THE LA/SA ISSUE?

Comment:

Why is Health Canada getting involved in the look-alike sound-alike issue instead of other issues related to medical/medication errors? How do the other issues relate to look-alike sound-alike health product names?

Response:

Longstanding unresolved issues relating to look-alike sound-alike (LA/SA) health product names, as well as a specific safety issue involving the potential for confusion between two approved biologics 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.

Various associations, 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.

Health Canada is participating in many areas to increase patient safety and to reduce medication errors through its work with the Canadian Patient Safety Institute and the Canadian Medication Incident Reporting System. The initiative to reduce the number of LA/SA health product names is just one of the ways that Health Canada is working to ensure the safety of Canadian patients.

The LA/SA health product name issue involves a number of concerned Directorates within the Health Products and Foods Branch (HPFB): Biologics and Genetic Therapies Directorate (BGTD), Marketed Health Products Directorate (MHPD), Therapeutic Products Directorate (TPD), Veterinary Drugs Directorate (VDD), Natural Health Products Directorate (NHPD) and the HPFB Inspectorate.

2.0 INCIDENCE OF MEDICATION ERRORS ATTRIBUTABLE TO LA/SA

Comment:

Is it not possible to use statistics from the available data that has been published to determine to what extent medication errors are attributable to name/name similarity? The percentage of LA/SA errors reported is not high given the number of products on the market. In addition, the relationship between the rate of reporting and number of actual errors is open to speculation. Why have studies not been done to get the Canadian "version" of the LA/SA issue?

Response:

In the United States, it is generally accepted by stakeholders, including sponsors, that LA/SA errors account for 25% of all medication errors.[1] It is also known that all medication errors, including LA/SA errors, occur much more frequently than they are reported. ISMP has published a list of known LA/SA errors in the U.S. As the majority of these drug names exist in Canada, it is reasonable to predict that the same errors would occur in Canada.

As a result of the development of the Canadian Medication Incident Reporting System, MHPD will eventually be in a position to obtain Canadian medication error data.

Based on the reports that have been received about LA/SA health product name errors, the growing number of new health products that are marketed each year and the increasing volume of patients who are prescribed medications, the incidence of LA/SA medication errors will continue to grow. In the interest of improving the quality of health, patient harm and death due to preventable error must be addressed and reduced. This can be accomplished, in part, by improving the safety of health products.

Comment:

Should the lack of recorded cases of LA/SA medication errors due to natural health products, veterinary drugs or medical devices not be investigated to determine why there is this difference? If there are no medication errors with these products due to LA/SA trade-marks, it may indicate that trade-marks are not the cause of medication errors for pharmaceutical and biological drugs but rather something else that is happening in the way pharmaceuticals and biological drugs are ordered and delivered.

Response:

Studies have not been conducted on look-alike sound-alike error in the area of veterinary medicine or natural health products. Regarding veterinary drugs, to date, there is no official mechanism in place to record medication errors for veterinary drugs. Based on experience and feedback from NHPD, the lack of recorded cases are due to a low reporting rate and not because these errors do not happen. Both VDD and NHPD believe that there is enough of a concern over this issue that they are both actively participating in the LA/SA WG to find a way to minimize the chance of medication errors due to LA/SA similarities.

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[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* 1999 Dec 37 (12): 1214-25.

Regarding medical devices, the visual appearance of the product alone indicates that there would not likely be medication errors resulting from LA/SA health product names. As a result, the Medical Devices Bureau has not, to date, been actively participating on the LA/SA WG.

3.0 OTHER FACTORS CONTRIBUTING TO MEDICATION ERRORS

Comment:

Medication errors are multi-factorial in origin. Factors that have been identified as causes of error include:

a) performance deficit;
b) failure to follow procedure;
c) transcription errors;
d) errors in documentation;
e) computer entry errors;
f) communication errors;
g) knowledge deficit;
h) distribution system failures;
i) written and oral orders that are confusing, incomplete or misunderstood; and
j) illegible or unclear handwriting.

Additional contributing factors include distractions, inexperienced staff, insufficient staff, and increased workload.

Response:

There is no denying that other factors cause or contribute to medication errors, however, if one were to deal with all factors at once, the task would be insurmountable.

Comment:

Will language differences/writing differences between individuals be taken into consideration with regards to the LA/SA issue?

Response:

HPFB intends to take individual language/writing differences into consideration. As outlined in section 4.4 of the *Issue Analysis Summary: LA/SA Health Product Names: The Development of a Comprehensive Policy Recommendation*, it is stated that "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."

4.0 SPECIFIC PROBLEM STATEMENT/IAS COMMENTS

Comment:

Clarification was requested on the following points of the problem statement and the IAS in general:

- Distinguish between what is within Health Canada regulatory activities and what is not, including context.
- Should the third bulleted point be included, excluded or modified?
- Where will other contributing factors be included?
- Address pre- and post-market issues (instead of "contain").
- Frequency should be considered and included in criteria.
- Pre- and post-market bullet needs to be clarified. Different interpretations are possible. Is the emphasis on "solution"?
- The aspect of risk should be clearly identified in the problem statement.
- Better definitions are needed overall.

Response:

All comments have been considered and will be incorporated into the revised problem statement or IAS, as appropriate.

Comment:

The use of the term "health products" does not capture/correspond to drugs, natural health products, veterinary drugs and, as such, should be made more specific.

Response:

By definition, health products include pharmaceuticals, biologicals, vaccines, medical devices, natural health products, radiopharmaceuticals and veterinary drug products.

5.0 INTERNATIONAL

Comment:

Health Canada should consider adopting systems that have been developed by the U.S. Food and Drug Administration (FDA) and the European Agency for the Evaluation od Medicinal Products (EMEA), since consistency with policies in other jurisdictions would be desirable in a global environment. Health Canada should also strive to align, as much as possible, its rules with widely accepted International Conference on Harmonization (ICH) and Veterinary Conference on Harmonization (VICH) recommendations.

Response:

In analyzing the LA/SA health product name issue, as outlined in the *Issue Analysis Summary: Look-alike Sound-alike (LA/SA) Health Product Names: The Development of a Comprehensive Policy Recommendation,* HPFB considered other national regulatory agencies' processes for reviewing health product names for LA/SA similarities and incorporated them into HPFB's proposed recommendations. As the LA/SA policy develops, HPFB intends to consider policies in other jurisdictions, as appropriate.

HPFB was represented at the two recent meetings in the U.S. regarding LA/SA drugs. In addition, Captain Thomas Phillips, Associate Director of the Division of Medication Errors and Technical Support in the Office of Drug Safety, was a guest speaker and contributed to discussions held at the LA/SA consultative workshop on October 20-21, 2003.

Health Canada has observer status at ICH & VICH and adopts ICH & VICH guidance documents, where possible, in order to achieve greater harmonization with other countries when regulating efficacy, safety and quality of health products. ICH (and VICH), at this time, has not undertaken to develop a guidance document to assess health product names for LA/SA similarities in the health product review.

Comment:

Health Canada's policy initiative proposes developing a framework for assessing a brand name during the review of a new drug submission. Multinational companies strive for global consistency in the branding of their products and do look rigorously for trade-marks that will not cause medical confusion/problems as well as those that can be used in most countries. A particular mark may offer safety benefits because it is a global trade-mark, an increasingly important factor with the spread of Internet use as a source of information.

Response:

Trade-mark identification alone has proven insufficient in preventing LA/SA health product name confusion. This may be because proposed trade-marks are considered and reviewed to determine whether they are confusingly similar from a marketing perspective (i.e. protect trade-marks from being used by others for financial gain) and not from a safety perspective (i.e. reducing medication errors). As stated by Dr. Levin (Director, Center for Medical Consumers) at the December 4, 2003 meeting of the Drug Safety and Risk Management Advisory Committee, "trade-marking has a legal aspect that is very powerful, and it has a marketing aspect that is extremely powerful. I don't mean to suggest that the safety is disregarded, but trade-marking is not a principle or a concept or an activity that

was developed in the field of safety management or risk management." Distinct trade-marks may reduce the incidence of medication errors due to safety but this is not always the case. For example, in the U.S., the top four most common LA/SA drug errors between May 2000 - 2002 involved drugs with registered trade-mark names:

Four Most Common Look-alike Sound-alike Medication Errors[2]

Sarafem® (fluoxetine hydrochloride)	Serophene® (clomiphene citrate tablets, USP)
Lantus® (insulin glargine [rDNA origin] injection)	Lente® Iletin® II (insulin zinc suspension, USP purified pork)
Serzone® (nefazodone HCl)	Seroquel® (quetiapine fumarate)
Depakote® (Divalproex Sodium)	DEPAKOTE® ER (Divalproex Sodium)

Furthermore, it is important to note that in Canada:

- Health product names are not required to have trade-marks.
- Trade-marks are not subject to regulation in the marketplace. For example, Industry Canada might refuse registration of a trade-mark but they cannot refuse the use of the name in the marketplace.
- If one company proposes two trade-marks that are similar, the similar trade-marks will be granted for both products.

Health Canada has no objection to the use of a global trade-mark so long as it does not create the potential for LA/SA medication errors within Canada.

Of note, the U.S. has been reviewing drug names for LA/SA similarities for the past decade. Currently, one third of proposed drug names are rejected because of LA/SA similarities.[3]

Health Canada intends to collaborate with other countries, particularly with the U.S., in its review of health product names.

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2 Matthew Herper. "FDA Takes on Drug Name Confusion." Forbes.com 5 December 2003. 2 January 2004 <http://www.forbes.com/2003/12/05/cx_mh1205confusion_print.html>

3 Patrick Sullivan, "New US labelling to eliminate drug conFUSION," Canadian Medical Association Journal, 4 March. 2003; 168(5) p. 598.

Comment:

Developing a new marketing platform to accommodate a unique Canadian brand name could potentially lead to increased costs, delays in product launches and ultimately, in availability of new drugs in Canada.

Response:

Policy development in this area will strive to respect the balance between safety and timely access. HPFB intends that the health product name review will occur concurrently with the product review and, for the most part, will not affect the timeliness of market authorization.

6.0 TRADE-MARKS

Comment:

Health Canada should be careful not to substitute its opinion for that of the recognized expertise of the Canadian Intellectual Property Office. Trade-mark lawyers use a rigorous process of trade-mark searches coupled with appropriate evaluation of the dispensing arena and, therefore, are in the best position to determine whether two trade-marks are confusingly similar. Proposed trade-marks that are confusingly similar to other trade-marks and terms, including LA/SA confusion, are rejected. Trade-mark applications are also screened and reviewed by an experienced examiner for potential confusion to other marks. The trade-mark process is self-policing in that companies have the opportunity to oppose each other's trade-marks or sue for infringement.

Response:

Health Canada, not Industry Canada, is ultimately responsible for ensuring the safety of a health product, including its name, as required under the *Food and Drug Act and Regulations*. The trade-mark process has proven insufficient in preventing LA/SA health product name confusion in Canada (refer to Section 5-International responses).

Comment:

From a marketing perspective, there may not be many choices (if any) to change brand names. The brand name that is preferred may more appropriately reflect the use of the product, may be better suited for marketing the product, or may be part of a global brand identity campaign.

Response:

At the FDA Drug Safety and Risk Management Advisory Committee meeting,

held on December 4, 2003, LA/SA issues were discussed in detail. The Office of Drug Safety's Acting Director, Dr. Paul Seligman stated that "our ultimate goal is to try to, to the degree we can, level the playing field and ensure that industry is taking these approaches and looking at trade names beyond just their commercial value and also to incorporate principles of safety and the consideration of safety in those processes."

Comment:

The final determination needs to recognize the benefits of the trade-mark as well as the risks. It must recognize that there are clear safety benefits to trade-marks which, unlike established names developed through the International Nonproprietary Name (INN)/United States Adopted Name (USAN) process, do not share common stems within classes, are generally shorter (and therefore, less subject to mispronunciation, misspelling, and the temptation to abbreviate), and are more easily remembered by health care professionals and patients.

The FDA has a formal process for trade-mark evaluation that has been in place for many years. We do not believe they claim that the medication error rate has declined nor are we aware of any statistics they have produced comparing the error rate before and after the system has been operational.

Response:

Trade-marks are designed to distinguish themselves from other marks but this does not necessarily avoid LA/SA confusion that may result in medication errors. For example, in a recent study that reviewed the cause of 469 fatalities due to medication errors, 5% of deaths were attributed to proprietary name confusion and 4% to generic name confusion[4].

The FDA has been reviewing drug names for LA/SA similarities for more than a decade. The reporting rate of adverse events, including medication errors is known to be low.

7.0 Legal

Comment:

One stakeholder group mentioned that they support regulatory oversight of product development that is based on sound scientific principles and good medical judgment supported by legal authority to legislate. Thus, it is fundamental that Parliament delegate

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[4] Jerry Phillips, "Retrospective Analysis of Mortalities Associated with Medication Errors," American Journal of Health System Pharmacy, 1 October 2001, Vol 58.

the authority to adopt and enforce the Policy. Voluntarily compliance is encouraged when legislative authority does not exist.

Response:

As stated in the LA/SA IAS, the *Food and Drug Regulations* would allow HPFB to adopt a pre-market requirement that the names of drugs not be likely to be confused 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 to result in safety concerns, then HPFB could refuse to issue a Drug Identification Number (DIN) [new drugs and drugs other than new drugs] and/or Notice of Compliance (NOC) [new drugs only], as applicable.

Upon becoming aware of a post-market safety concern associated with LA/SA name confusion, following issuance of an NOC and/or DIN for a drug, 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.

8.0 SCOPE/PRIORITIZATION

Self-Care/OTC Products

Comment:

There is little evidence to support the need to apply this policy beyond prescription drugs and biologics, since the selection and use of self-care products has very little in common with the way prescription drugs and other higher risk products are administered to patients. As a result of features such as distinctive and clear labeling and differentiated product display, along with the consumer's self-driven selection process, there have been only rare instances where Health Canada has had concerns over self-care product names that have resulted in products being re-named or withdrawn. Such cases are few and the current approach has proven itself to be adequate for public safety.

Response:

At the October 20-21, 2003 LA/SA consultative workshop, respondents believed that the LA/SA health product name project should be prioritized as follows:

1. Prescription drugs for human use (including Schedule C, Schedule D and Schedule F drugs)
2. Over-the-counter products for human use
3. Natural Health Products for human use

4. Veterinary Drugs
5. Medical Devices

The respondents general rationale for prioritization was based on:

- risk to human health;
- magnitude of harm (i.e. prescription drugs are more closely controlled for a reason);
- consumer protection;
- incidence and frequency;
- most information available (some problems identified); and
- ability to address / regulate.

The outcome of the workshop concurs with the LA/SA IAS identification of the need to focus specifically on LA/SA issues that appear to pose the most potential for health risk. The LA/SA IAS states that the first priority is to implement both the pre-market and post-market recommendations for Schedule C, D and F drugs. Certain issues that are common to over-the-counter drugs, such as product -line extensions, will need to be considered.

Susan Winckler (Vice President, American Pharmacists Association) stated at the June 23, 2003 meeting, entitled *Minimizing Medication Errors- Methods for Evaluating Proprietary Names for Their Confusion Potential*, that "drug name safety testing for all medications — regardless of their class — should be held to the same high standards. Medication errors due to name confusion can occur with proprietary and nonproprietary prescription drugs, as well as OTCs. Consumers selecting an OTC may select the incorrect product due to confusion generated by similar product names or brand name line extensions. Eliminating confusing nomenclature practices for all medication products is an important step towards reducing medication errors of all kinds."

Generic vs. Generic Products

Comment:

Is there a way that we could have an impact on International Nomenclature?

Response:

Health Canada does not have representation on either the INN committee or the USAN committee that are responsible for approving proposed generic names and, based on membership requirements, it is unlikely that Health Canada would be able to obtain representation. However, INN proposed names are published for consideration in the *WHO Drug Information* publication and USAN names under consideration are published on the USAN website and USP Pharmacopeial

Forum. All of these publications provide Health Canada with the opportunity to comment on suggested USAN names.

Comment:

Generic vs. generic LA/SA similarities should be a priority.

Response:

At the Advisory Committee on Management (ACM), when asked to list examples of LA/SA health product name errors, the participants more often gave examples of "Brand name versus Brand name confusion," followed by "Generic versus Generic name confusion." HPFB realizes that "generics versus generics" are an issue, however as Health Canada does not have much of an influence on requiring a change to international generic names (INNs, USAN names), this issue will be a second priority.

The LA/SA WG believes that preventive measures could be implemented to reduce errors between similar generic drugs (i.e. "tall man" letters, the use of capital letters in the middle of words on labels to emphasize that portion of the word). This is currently a strategy that the US FDA is using to respond to similar generic names.

Different Brand Names - Similar Active Ingredients

Comment:

Different brand names with similar active ingredients may be another policy issue to consider.

Response:

As stated in the LA/SA IAS, since different brand names for the same active ingredient often occur between companies and are unavoidable, the issue of different brand names for the same active ingredient within the same company is not significant. In addition, there is little evidence to suggest that there is a significant health risk if this type of error does occur. As a result, the LA/SA WG will not be focusing efforts on this issue.

Definitions of Types of Health Product Names

Comment:

If the scope is going to include health products, then the following must be defined:

- Common names
- Generic names
- Proper name
- Latin name

Response:

The LA/SA IAS defined common names, generic names and proper names in section 3.1 - Definitions. With the exception of natural health products, Latin names are not routinely used by stakeholders to identify health products. When the LA/SA project focuses more specifically on natural health products, the definition for Latin Names will be added, as applicable.

Natural Health Products

Comment:

Natural Health Products and over-the-counter (OTC) products should be grouped together with regards to LA/SA, as the issues are very similar.

Response:

HBFB will consider aligning the policy for natural health products and OTC products, when possible. Natural Health Products are regulated under the *Natural Health Products Regulations* while OTC drugs are regulated under the *Food and Drug Regulations*.

Human Drugs Used for Veterinary Drugs

Comment:

Human drugs used for veterinary uses were not considered in the LA/SA IAS prioritization list.

Response:

This issue will be incorporated into the revised IAS.

9.0 OPTION ANALYSIS

Comment:

Workshop participants believed that screening criteria should include:

- a system that has been validated

- a solution that is transparent
- a solution that involves shared responsibility of stakeholders
- timeliness as a screening criteria; and
- comparative criteria of cost/benefit.

Response:

Section 12 of the LA/SA IAS addresses timeliness of health product review, while Section 19 discusses validation issues. Cost/benefit to all stakeholders was considered by the LA/SA WG and is referred to in Appendix B Look-alike Sound-alike Options (pre- and post-market).

HPFB is committed to being transparent in its recommendations.

10.0 RECOMMENDATIONS

Comment:

A multi-faceted approach should be undertaken.

The different review layers that have been proposed by Health Canada appear to have the potential to introduce new levels of subjectiveness. Will the elements of the options unfold sequentially or in parallel?

Response:

A multi-faceted approach to respond to LA/SA health product names has been proposed and that they unfold sequentially.

Pre-market, Health Canada is proposing the use of a complex computer application to ***objectively*** analyse and identify health product names for LA/SA potential. If a health product name is flagged for potential LA/SA similarities the name will be reviewed by a Health Canada reviewer. The process of using an individual's expertise and judgement is, by its nature, a subjective process. However, the reviewer will have a policy to follow that should result in a fair, systematic and consistent method of assessing LA/SA health product names. If the reviewer cannot come to a decision, the health product name will be considered further by an Interdirectorate Name Review Committee.

Post-market, Health Canada is proposing that health products should be monitored for LA/SA similarities (i.e. through media scans, medication error reports etc.). When LA/SA health product names are identified post-market as a concern, it is anticipated that sponsors will be given an opportunity to provide alternative solutions to a name change when a LA/SA health product name arises.

Comment:

We are concerned about filing a prioritized list of name choices to Health Canada. Submitting a prioritized list should be optional. If a prioritized list is submitted, how will it be used, i.e. will all the names be checked or will they be examined one by one?

Response:

A prioritized list has been suggested in order to reduce delays. It is up to the sponsors as to whether they would like to file one proposed name or more. If filing more than one, a "sponsor created" prioritized list of name choices could be provided. If the first proposed name is rejected, HBFB would be able to start reviewing the second name on the list promptly.

Comment:

Will there be an appeal process if the sponsor does not agree with Health Canada's conclusions on the trade-mark?

Response:

A sponsor has the right to appeal name review decisions*. When a sponsor disagrees with a Health Canada decision regarding a submission review, they may appeal the decision. The Health Canada Policy *Appeals Procedures for Drug Submissions* may be referred to for more information regarding appeals. <http://www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/appeals_policy_e.pdf>

*** This is assuming that the name review will occur during the submission review**

Comment:

Industry and Health Canada (HC) share a common objective: the well being of the Canadian patient. In that perspective, we are supportive of Health Canada's initiative to reduce the risk of medical errors in prescribing, dispensing or administration of a product. It is good that Health Canada is being proactive about this issue.

Response:

The name of a product is that which identifies it as unique from all other products, therefore, it is in the best interests of all stakeholders, including Health Canada, sponsors, health care professionals and patients, that health product names not be confused with one another. A consistent, formal process will allow Health Canada to review health product names for LA/SA similarities in a fair, equitable and transparent manner.

Comment:

A) We support a combined approach including:
Policy, Complex Computer application, Name review/name review committee/company provides name analyses

B) We support a combined approach including: Policy, computer related, industry requirements, monitoring and health promotion.

C) ISMP Canada endorses the need for establishing a process of review of health product names in Canada and commends Health Canada's initiative to develop a program that will systematically and pro-actively evaluate the potential for error with new product names.

D) Policy development approach is a preferred approach by industry.

E) We need to promote safe practices for minimizing name confusion including existing names.

Response:

With appropriate pre-market and post-market processes in place within HPFB to respond to potential LA/SA health product names, the risk of health product name confusion should be reduced.

It is important that all stakeholders, including sponsors, work together to minimize the potential for confusion between products with names that look or sound alike.

Comment:

Other suggestions to address look-alike sound-alike health product names included:

- The inclusion of Package and labelling in policy on new product requirements.
- The inclusion of bar coding as a requirement on packaging of new products.
- Electronic prescribing
- The monitoring option include requirements for name changes made in the U.S. by pharmaceutical companies.
- Links to other related initiatives and compatibility, e.g. medication error program, electronic prescription, bar coding, successor systems.

Response:

The issue of look-alike packaging and labelling is outside the scope of this policy initiative and may be addressed at a later date.

Bar coding is a measure that could be used to help prevent medical error and was considered as a post-market option in the LA/SA IAS. The pros and cons to this option are outlined in the LA/SA IAS Appendix B: post-market option #4. In the analysis of this option, the LA/SA WG concluded that bar coding has a number of drawbacks including the following:

- it cannot be a standalone solution since errors can happen upstream from bar coding (i.e. when an Rx is written and misunderstood by the pharmacist); and
- significant stakeholder investment would be required in bar coding. The Regulatory Policy specifically states that "information and administrative requirements are limited to what is absolutely necessary and imposes least possible cost."

The FDA estimates it will cost U.S. hospitals more than $7 billion US to implement bar coding technology.[5]

The use of bar codes are not a guarantee that error will not occur. For example, recently a California health care agency labelled thousands of prescriptions incorrectly due to a computer error. <http://www.mercurynews.com/mld/mercurynews/news/5418874.htm>

Electronic prescribing was considered as a post market option in the LA/SA IAS. The pros and cons to this option are outlined in the LA/SA IAS Appendix B: post-market option #5. In the analysis of this option, electronic prescribing had some of the same drawbacks as bar coding.

Health Canada, in its post-market LA/SA policy, has seriously considered and intends to actively monitor LA/SA health product name changes that are made in the United States.

Where relevant, the LA/SA health product name project will consider links to other related initiatives (i.e. medication error program electronic prescribing).

Comment:

The issue/question of voluntary vs. mandatory reporting on available data still needs to be addressed.

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[5] Stephen Nicolls, "Eliminating drug name mixups target of new federal program", Medical Post, 13 January 2004; Canadian Medical Association Journal, 4 March. 2003; 40(2) p. 1.

Response:

The issue of voluntary vs. mandatory reporting is outside the scope of the LA/SA issue. Where there is more reporting of medication errors, Canadian statistics related to medication errors attributable to LA/SA could be developed.

11.0 LA/SA COMPUTER APPLICATION

Comment:

Will the computer application be designed to select similarity to any degree or to some arbitrary degree? The current proposal lacks sufficient detail concerning the parameters to be used in a computer-based analysis. The computer application should include spelling/phonetics, frequency, route of administration, labelling and packaging. Although "complex computer applications" hold promise in the area of identifying possible look-alike/sound-alike issues, such systems are still in a relatively early stage of development. It is important to be careful of over-reliance on the computer system. More is needed than computer applications: computer analysis *and* "qualitative" expert analysis.

Response:

Currently, the U.S. FDA uses a computer application that applies proven linguistic methods (i.e. Edit Distance, Soundex, DICE, LCSR, Aline) of comparing names for orthographic (spelling) and phonetic or phonological (pronunciation) similarities. The similarity of health product names is determined based on score results. Furthermore, this application considers similar strengths and dosage forms when looking at a name.

For more information regarding these linguistic measures, please refer to LA/SA consultative workshop presentations given by Dr. Greg Kondrak <http://www.hc-sc.gc.ca/hpfb-dgpsa/bgtd-dpbtg/g_kondrak_e.html> and/or Dr. Bruce Lambert <http://www.hc-sc.gc.ca/hpfb-dgpsa/bgtd-dpbtg/b_lambert_e.html>.

HPFB has not yet acquired a computer application; however, parameters used in the computer-based analysis will be similar to those used by the FDA.

A multifaceted approach is proposed for the name review process. As outlined in the LA/SA IAS, the computer application is being proposed as a screening tool to identify potential LA/SA similarities. Names that are flagged will be reviewed by a Health Canada reviewer. If the reviewer cannot reach a decision, the name will be considered further by an Interdirectorate Name Review Committee. In addition, a sponsor will be required to show, within the submission, that a proposed health product name does not have LA/SA name similarities.

Comment:

Computer systems should only be used as a tool to aid in the determination of whether there is medication error potential based on many other factors. A complex computer application may not be necessary if the company has already spent time and resources in searching the names. Will Health Canada's computer analysis supersede the conclusions provided by the sponsor?

Response:

It is envisioned that the computer application will serve as a screening tool; a precursor to a name review. If the sponsor has provided a thorough and complete analysis, Health Canada's analysis should coincide with the sponsors' conclusions.

Comment:

If a computerized system is developed or acquired by Health Canada, it should be made available to the sponsors to use prior to submission of names to Health Canada for approval.

Response:

This will be considered and Health Canada will work toward making the computer application available to sponsors.

Comment:

A computer application might be too costly and may take too long to implement.

Response:

Cost and implementation time will be taken into consideration when evaluating potential computer applications.

12.0 REVIEW TIME

Comment:

How will this policy initiative impact overall drug submission review times in Canada? Adding a new criterion to drug approval will further complicate and lengthen the process. Depending on the option chosen and the details developed, there may be a significant impact to industry, both in the application of any potential policies plus in extra time added during the review process.

Response:

The 2003 Budget allocated $190 million dollars over 5 years in order to "improve timeliness of HC regulatory processes with respect to human drugs, while preserving the principle that safety is of paramount concern."

HBFB, through the Therapeutic Access Strategy (TAS), is committed to reducing drug review times. It is anticipated that the health product name review will occur concurrently with the rest of the product review. In most cases, the health product name review will have no impact on review times. The U.S. currently has a 60 day review target to review a proposed health product name.

It is acknowledged that the LA/SA health product name initiative will probably result in additional filing requirements to ensure that a health product name is not likely to be unsafe due to its potential to be confused with other products with similar names.

13.0 TIMING OF NAME REVIEW

Comment:

It has been recommended by some stakeholders that Health Canada evaluate brand names much earlier than at the new drug submission stage, in order to provide Canadian subsidiaries of multinational companies time to address name issues. Industry does not want name issues to be identified at the end of the review during the labelling stage.

Response:

This concern is understood and this recommendation will be considered when developing LA/SA policy and related processes.

Health Canada is committed to ensuring that the name review will occur at a time that is of greatest convenience to all stakeholders. It is recommended that the sponsor take precautions to eliminate the potential for LA/SA names before the proposed product is submitted for approval.

Comment:

We consider it critical that the brand name look-alike sound-alike issue be resolved prior to market introduction. We hope that Health Canada understands the potential limitations on our part and the cost incurred when changing brand names and re-establishing a brand.

Response:

Health Canada concurs with this suggestion, since it is in the best interests of

stakeholders, health care practitioners and consumers that health product names not be prone to confusion either through LA/SA similarity or through re-introduction as a new name.

14.0 POST-MARKET - CHANGING BRAND NAMES

Comment:

Once marketed, there is significant brand equity and brand identity developed which would all be lost if we had to change the name.

Response:

Health Canada has considered the costs to a sponsor of changing a product name post-market. The pros and cons to this option are outlined in the LA/SA IAS Appendix B: post-market option #6. In the analysis of this option, it was concluded that 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.). All effort will be made to resolve the potential LA/SA health product name pre-market. Since the health and safety of Canadians is of foremost importance for Health Canada, as a last resort, a name may need to be changed or modified to avoid confusion.

Comment:

With regards to the review of marketed products (and post-marketing), we hope there is the opportunity to negotiate and state our case for maintaining a specific brand name.

Response:

Post-market, sponsors will be given an opportunity to provide alternative solutions to a name change when a LA/SA health product name issue arises.

15.0 STAKEHOLDER INVOLVEMENT

Comment:

Health Canada should obtain stakeholder input on how to implement the LA/SA name review. The current proposal lacks sufficient detail concerning the criteria for sponsor-generated data submissions. Specific details need to be provided on what will happen when two similar product names are being reviewed at the same time (i.e. what happens to submission A that is filed later, as well as confidentiality issues). Recommendations should include specific criteria for name acceptability.

Please ensure that the final published report does clearly outline these next steps. We would like to ensure that any policy development regarding this issue will be transparent and open.

Response:

Health Canada is committed to public consultation, transparency and openness in policy development. The decision-making framework, that Health Canada uses to develop policy, reflects the involvement of interested and affected parties throughout its three phases that include: issue identification (identify the issue and put it into context); risk assessment (assess risks and benefits); and risk management (identify and analyze options; select a strategy; implement the strategy; and monitor and evaluate the results).

Prior to developing significant details of specific options and recommendations, Health Canada sought confirmation from stakeholders regarding the direction of the LA/SA project, as outlined in the LA/SA IAS.

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 20th and 21st 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.

Further consultation activities will be planned once all comments have been analysed, a revised LA/SA IAS is complete and a draft LA/SA policy has been developed. Sponsor submission requirements, post-market and implementation details etc. will be developed and proposed as Health Canada moves forward in its development of a policy; as outlined in the decision-making framework.

The final LA/SA IAS will clearly outline the next steps on the LA/SA project.

Comment:

ISMP Canada will continue its post-market monitoring of incidents and will continue to be available for consultation. ISMP Canada is prepared to play a role in a formalized program of pre-market review of product names.

Post-market review could involve drug companies, especially in cases of LA/SA alerts. We would like to ensure that there will be further opportunities for industry to comment.

Response:

Cooperation and teamwork from all stakeholders will enable this initiative to be successful. It is only through recognition of the issue and active involvement in steps to reduce LA/SA names that the full scope of this objective will be realized.

Comment:

Would it be useful to have reps from the companies who come up with brand names to be at the table? They need to be involved in the process.

Response:

Health Canada invited all relevant associations that represent industry to the October consultative workshop. Of those invited, the following associations were represented:

- Canada's Research Based Pharmaceutical Companies;
- Groupement provincial de l'industrie du medicament;
- Natural Health Products Manufacturer's of Canada;
- Non-prescription Drug Manufacturer's Association of Canada; and
- The Canadian Generic Pharmaceutical Association.

Of those invited, the following were not able to attend:

- BIOTECanada;
- Canadian Health Food Association; and
- Canadian Homeopathic Pharmaceutical Association.

In addition, the LA/SA issue was presented and discussed at the Advisory Committee on Management on October 1, 2003. Sponsor representation included participation of the following sponsors or associations representing sponsors:

- Aventis Pasteur Limited;
- Canada's Research Based Pharmaceutical Companies; and
- Novopharm

During the consultation period, all stakeholders were invited to comment on the draft LA/SA IAS.

16.0 EDUCATION OF HEALTH CARE PROFESSIONALS

Comment:

Will there be an opportunity for an educational or awareness effort directed to healthcare professionals and will this presumably lead to a lesser potential for confusion and prescribing errors?

Response:

The fact sheet entitled "Look-alike Sound-alike Health Product Names" outlines what stakeholders can do to reduce the incidence on medication errors due to LA/SA similarities. This document is available on the Biologics and Genetic Therapies' website at:
<http://www.hc-sc.gc.ca/hpfb-dgpsa/bgtd-dpbtg/lookalike_soundalike_factsheet_e.html>

Health Canada advocates educational and awareness efforts directed at health care professionals and other stakeholders and encourages stakeholders to become involved in educating healthcare professionals in order to reduce the incidence of medication errors. Promotion and monitoring of the LA/SA issue is one of the measures that has been deemed necessary for the success of this initiative. Since the healthcare industry has an increasing volume of patients, especially elderly patients, it is important that the risk of confusion also be lessened by ensuring that health products have names that will not be confused with one another.

17.0 RISK MANAGEMENT

Comment:

A) Risk management plans both pre- and post-approval are very important to avoid the potential name change scenarios occurring in the U.S.

B) We do not believe a risk management program should become routine for all trade-marks. In certain limited cases, where the risk of error can be reasonably established and an intervention will likely reduce such risk to a level that reasonably avoids the risk, a specific, limited, risk management program does appear appropriate.

Response:

At the December 4, 2003 FDA Drug Safety and Risk Management Advisory Committee Meeting, two questions were posed that relate to the issue of whether or not OTC products should undergo a name review. These questions were as follows:

1. Is it possible to triage the drug names into groups that may be handled differently based on risk?

2. Describe circumstances, if any, when it would be appropriate to approve a proprietary drug name contingent on a risk management program being in place.

In response, it was agreed that all drugs should be reviewed because the FDA does not know which ones will pose a problem. Even if a drug appears innocuous, it may not be if another product is used in error.

A name change, especially pre-market, may be the most effective route of risk management in some LA/SA health product name cases.

Post-market, it is anticipated that sponsors will be given the opportunity to provide alternative solutions to a name change when a LA/SA health product name issue arises.

Comment:

Any risk management system imposed upon approval is of unknown value because it is based on speculation about the risk of error, supposition about the role of the trade-mark with regard to the assumed risk, and presumption that the prescribed intervention will have a positive outcome.

Response:

Based on the precautionary principle, Health Canada cannot use scientific uncertainty where safety is a concern as reason not to act.

Health Canada has a responsibility to assess the safety of a health product and to endeavour to prevent LA/SA health product name errors. Health Canada is confident that effective policy and risk management to prevent LA/SA medication errors will have a positive outcome.

18.0 DATA EVALUATION

Comment:

If sponsor-generated data are submitted to Health Canada, how will the data be evaluated? And, how will Health Canada determine adequate sample size for evaluating similarities in trade-marks?

Response:

A proposed name will be evaluated for LA/SA similarity against existing and other proposed health product names. Decisions and direction regarding criteria for sponsor-generated data submissions will be provided as the policy is developed and as the science develops to assess outcomes data.

The FDA has been reviewing proprietary names for potential LA/SA similarities for the past decade and is still grappling with these same issues. Current FDA methods to evaluate proprietary drug names represent process-based science. An outcomes based scientific method has yet to be developed. The June 26, 2003 meeting entitled *Evaluating Drug Names for Similarities: Methods and Approaches Public Meeting,* co-sponsored by the FDA, the Institute for Safe Medication Practices (ISMP) and the Pharmaceutical Research and Manufacturers Association (PRMA), attempted to explore current methods and approaches to evaluate proprietary drug names. The following question was posed to participants:

1. In studies designed to evaluate potential prescription errors, what is an appropriate study design and what is the appropriate size for a prescription drug study?

As a follow-up to this meeting, the FDA Drug Safety and Risk Management Advisory Committee considered these same issues in a public meeting held on December 4, 2003. In order to move forward on these issues, the committee suggested that the FDA hold a meeting with representatives from the Pharmaceutical Research and Manufacturers of America and other stakeholders to address this issue further regarding data requirements. Health Canada will be considering the outcomes of these discussions.

19.0 VALIDATION

Comment:

The objective of this initiative states: "With processes in place, the morbidity and mortality resulting from medication errors should be reduced." On what basis can this conclusion be supported? How will the program be validated to ascertain that potential dispensing errors are indeed avoided? Existing methodologies for testing trade-marks for medication error potential (e.g. verbal and handwriting tests, expert committees) are subjective in nature, qualitative not quantitative, prone to bias, and do not achieve replicable and verifiable results. Without proper validation, neither the sponsor data nor the computer analysis will provide meaningful conclusions regarding the potential for medication errors.

Response:

At this time, Health Canada does not have the answers to these questions.

The FDA Drug Safety and Risk Management Advisory Committee considered validation issues in a public meeting held on December 4, 2003. In order to move forward on these issues, the committee suggested that the FDA hold a meeting with representatives from the Pharmaceutical Research and Manufacturers of America and other stakeholders to address the validation issue further. Health Canada is interested and will consider the outcomes of these discussions.

Of note, the FDA computer application uses linguistic principles to produce reliable and validated lists of LA/SA similarities.