Look Alike Sound Alike Drug Name Review: Health Canada Guidance

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INTELLECTUAL PROPERTY LAW
Regulatory Legislation

**Food and Drugs Act/Regulations:**

- prohibits sale of a drug in any manner that is likely to “create an erroneous impression regarding its safety”

- requires a manufacturer to file a new drug submission containing “sufficient information and material” to enable Health Canada to assess safety and effectiveness of the drug, “including a statement of the brand name”

- prohibits a manufacturer from selling a new drug unless a drug submission is filed and a NOC or DIN is issued

**Not clear:**

- what information must be contained in drug submission with respect to brand name

- whether Health Canada can refuse to issue NOC or DIN if confusion with another drug name considered likely to result in safety concerns
Discussions and Draft Policy Papers

• Within Health Canada, issue of LA/SA drug names longstanding issue

• HC realized LA/SA drug names a serious health and safety concern, but internal doubts as to whether it had authority to enforce name restrictions under Food and Drugs Act and Regulations

• 1992 - two draft policy papers recommending changes to use of abbreviations in brand name drugs and use of brand names similar to generic names; neither was implemented

• 1995 - Health Canada developed a draft policy regarding product line extensions; not implemented as consensus could not be reached

• Continued to evaluate proposed product names on a case-by-case basis
LA/SA Product Names - “Issue Analysis Summary”


• review of LA/SA product names was inconsistent and arbitrary
• no computer system set up to flag identical or similar names
• questionable whether Food and Drugs Act/Regulations could be used to require a name change
2006 Guidance for Industry: Drug Name Review – LA/SA Health Product Names


- To provide clarification regarding submission of proposed drug names and reduce risk of medication errors due to LA/SA drug names

- Applies to all prescription drugs (as of January 1, 2006) and (as of July 1, 2006), natural health products, medical devices, OTC drugs, and veterinary drugs

- Health Canada *Health Products and Food Branch* (HPFB) put in charge of reviewing proposed drug names

- Guidance interprets *Food and Drug Regulations* to permit HPFB to refuse to issue a DIN or NOC if confusion considered likely and could result in safety concerns
Three specific naming practices to be discouraged:

• Similar brand names that do not contain the same active ingredients

• Brand names similar to generic names which contain different active ingredients

• Product line extensions by using brand name of another drug together with a modifying prefix or suffix, when extension contains different active ingredients than established product
2006 Guidance for Industry

Brand Name Submission

Brand name submission of manufacturer must contain:

• the proposed brand name of the drug;

• a prioritized list of alternative names with a maximum of two alternatives; and

• a risk assessment of product’s brand name supported with studies, data and analysis, including *but not limited to*:
  – Search for similar proprietary/nonproprietary names (drug/medical reference search)
  – Computer analysis (orthographic/phonetic);
  – Prescription testing studies (oral and handwritten)
  – Medication error literature (including possibility of error based on dosage form, route of administration, end users, etc)
HPFB considers following contributing factors during review process:

- Marketing status (RX or OTC);
- Therapeutic category;
- Indications and direction of use;
- Clinical setting for dispensing or use (inpatient or outpatient hospital or clinic vs. retail pharmacy);
- Packaging and labeling; and
- Strength; dosage form;
- Proposed dose
- Similar patient populations
- Storage

If one or more of above are different, potential for confusion minimized and less concern with brand name and risk of medication error
2006 Guidance for Industry
Brand Name Review Process

- Once submission received, HC completes initial review of name within a 90 day target.

- Due to possibility that another product name is approved between time of initial name review and final approval of product name, HC conducts second abbreviated review focusing on proprietary names approved from time of first review - Second, abbreviated review of name conducted within another 90 days.

- If more than one submission proposes same/similar brand name for different products, HC works with sponsors to facilitate a satisfactory solution. In event this does not occur, HC will proceed with approval of all submissions, and when “first drug submission approved” others asked to change name.
Pre-Market Drug Name Submissions

- Drug name submissions are confidential
- Cannot obtain details on pre-market cases of potential confusion identified during drug name submissions process
- Rates of rejection/approval not currently tracked
Post-Market Reports
LA/SA Drug Name Confusion

• Health practitioners can report an incident of LA/SA confusion through Canadian Medication Incident Reporting and Prevention System (CMIRPS)

• CMIRPS works with Health Canada and associated agencies to collect incident reports and inform health practitioners and the public of the risk of confusion between drug names

• Doctors and other health practitioners are expected to report any incidences through Health Canada’s Canada Vigilance program

• Members of the public can report incidents through Health Canada’s Healthy Canadians website

*Food and Drug Regulations* provide authority for Health Canada to stop sales of a drug if potential health risk is identified
Post-Market Examples
LA/SA Drug Name Confusion

• **2002** - Health Canada published report involving confusion between Astra-Zeneca’s antipsychotic drug **SEROQUEL** and Bristol-Myers’ **SERZONE**; NO FURTHER ACTION TAKEN; SERZONE DRUG SUBSEQUENTLY REMOVED FROM MARKET FOR UNRELATED REASONS

• **2004** - Janssen-Ortho and Aventis Pharma released joint safety bulletin regarding mix-ups between the Alzheimer’s medication **REMINYL** and the diabetes medication **AMARYL**. 2005 ORTHO NAME CHANGE FROM REMINYL to RAZADYNE in U.S DUE TO LA/SA ISSUE

• **2010** - Health Canada published a letter from Novartis detailing confusion between **MAALOX MULTI-ACTION** and other liquid products; NO FURTHER ACTION TAKEN

• **2011** - Health Canada published a letter from Boehringer Ingelheim and Sanofi-Aventis regarding instances of confusion between **PRADAX** and **PLAVIX**. JANUARY 2013, BOEHRINGER VOLUNTARY NAME CHANGE TO PRADAXA

• **2013** – ISMP Canada’s consumer reporting program (safemedicationuse.ca) received a report regarding elderly patient who mistakenly received BISOPROLOL instead of BISACODYL from a pharmacy; NO FURTHER ACTION TAKEN
2013 Draft Revised Guidance for Industry Review of Drug Names for LA/SA Attributes


• Reviewed experience of drug name approvals since 2006 and found significant variation in amount, type and quality of evidence submitted

• Goal to provide more detailed direction on the testing procedures to be used and the information to be submitted to HC, with expressed objective to reduce medication error

• Applicable to biologics and both prescription and non prescription pharmaceuticals for human use
New Draft Guidance on LA/SA Drug Names
No concern with veterinary products?
2013 Draft Revised Guidance for Industry
Initial Brand Name Review- The 14 Questions

Initial Review requires sponsors to respond to 14 questions

Questions 1-8:

• If affirmative reply to ANY of questions 1-8, HC will not initiate brand name review; sponsor must submit new name

• Sample questions 1-8:
  
  – Does name include or imply an ingredient not included in the drug product?

  – Is name identical to an authorized product in Canada containing a different medicinal ingredient?

  – Does name suggest an unsupported route of administration i.e. Acetaminophen Oral for a suppository product?
Questions 9 – 14:

- IF affirmative reply to ANY of questions 9-14, will raise concern that proposed name could result in confusion, but HC will continue its review if sponsor wishes

- Sample questions 9-14:

  - Was the same/similar name used previously for a product no longer available on the market?

  - Has name been approved in another country for a product with a different medicinal ingredient?
If proposed name not refused, sponsor must conduct a three-step assessment of proposed drug name for LA/SA similarities:

“Search, Simulate and Synthesize”
“Search, Simulate and Synthesize” Visual Chart

1. SEARCH
- Search proposed name against drug databases
- Identify any name with similarity score of 65% or above
- Search published literature for error reports

2. SIMULATE
- Develop medication-use process map(s) for proposed name
- Test proposed name in screen-based simulations of auditory perception, visual perception, short-term memory
- Conduct medication-use process simulations encompassing prescribing, transcribing, selection, dispensing, administration and self-selection

3. SYNTHESIZE
- Document names that have been identified as confusing during steps 1 and 2
- Inclusion of names in FMEA process
- Conduct FMEA
- Document results
- Prepare final report with rationale and recommendation for approval

HEALTH CANADA

INITIAL BRAND NAME REVIEW
Screen proposed name according to general safety criteria

REVIEW
- Search proposed name against health product databases including the Drug Submission Tracking System (DSTS)
- Review sponsor’s detailed LASA brand name assessment
- Request additional information, if needed
- Decide on the acceptability of the proposed brand name

ACCEPT REJECT
Step 1: “Search”

- **search drug name and medication error databases** to identify existing drug names that may have potential for confusion with proposed brand

- **include medication error reports in published literature** if proposed name already in use in another country

- **submit proposed brand name to health product search engine** and identify any name with a similarity score *equal to or greater than 65%* using the ALINE algorithm (objective criteria for orthographic, phonetic and combined orthographic-phonetic similarity)

- In addition, submit 5 names with highest phonetic similarity and 5 with highest orthographic similarity to proposed name (regardless of whether their ALINE similarity score is greater than 65%)

- **Submit any prior name assessment report** and results provided to an international regulator for proposed name

- **HC conducts its own database searching** for potentially confusing brand names
Step 2: “Simulate”

sponsors must conduct **two simulation tests** to assess risk of confusion:

1. **Screen based simulations - psycholinguistic testing**
   - includes visual perception tests, auditory perception and short term memory tests

2. **Medication use testing**
   - sponsors must prepare and submit a process map describing where and how brand name will be used based on its indications, and who will come into contact with product
“PSYCHOLINGUISTICS”
What is it??

• the study of mental representations and processes related to composing, comprehending, speaking, hearing and remembering language

• looks at what cognitive processes are involved in the ordinary use of language
Psycholinguistic Testing...

- screen-based tests of a proposed brand name in auditory perception, visual perception, and short-term memory tasks

- focuses on confusability in the three cognitive domains most often implicated in name confusion errors: vision, hearing and short-term memory

- considered easy to control, efficient and thought to produce objective results
Medication Use Testing
What is it??

- requires proposed name to be communicated and processed as it would in real-world circumstances

- uses real-life participants--doctors, nurses, nurse practitioners, pharmacists, pharmacy assistants/technicians, secretaries, patients—to simulate interaction with the drug

- extent of simulation testing depends upon the type of product being tested (i.e. injectable drug used only in operating room setting v. oral prescription drug)

- results of studies identify the potential hazards, errors, and failure modes related to use of name.

- information is collated and assessed in the last step of the name review process: Synthesize
Step 3: “Synthesize”

“Synthesize”:

• Sponsors must conduct a **Failure Mode and Effects Analysis (FMEA)** - synthesize information gathered and demonstrate that proposed name has no significant failure modes

• Sponsors must prepare report summarizing all findings generated through 3 step analysis and submit to HC

• HC renders decision to reject or approve name

• HC consideration of LA/SA drug name issues different from *Trade-marks Act* - HC focus is on mistakes; not confusion as to source – brand name may be registered as a trade-mark but disallowed for sale by Health Canada
Consultation with Stakeholders

• Draft Revised Guidance published February 19, 2013

• Open to comment until April 19, 2013

• Health Canada met with individual industry stakeholders
Primary Industry Concerns

• Psycholinguistic testing - too stringent and exacting compared to regulations of other countries

• Simulation testing should not require the inclusion of consumers

• HC should review more than one name at a time
Health Canada’s Response

HC indicated it may revise Guidance document taking into account some of the comments received:

• may move requirement for psycholinguistic testing to an appendix to the Guidance as “optional”

• considering whether sponsors can submit more than one name at a time
New Guidance:  
A step toward clarification?

• Health Canada considers the 2013 Draft Revised Guidance a significant step towards clarifying what is expected of sponsors, taking into considering its experience over past seven years

• Final version expected late fall 2013/early winter 2014

• Proposing a transition period of at least ONE YEAR from the old to the new Guidance and HC will not enforce new Guidance until end of that period
Proposed Amendments to
Food & Drugs Regulations

• **June 22, 2013** - Health Canada published proposed amendments to *Food and Drug Regulations* as part of its “Plain Language Labeling Project” for labeling prescription and non-prescription pharmaceutical and biologic drugs for human use

• Regulatory proposals include, among other items, a requirement that a new drug submission contain an assessment as to whether there is a likelihood that the new drug brand name will be mistaken for another similar brand name

• Would codify the LA/SA Guidance and formalize authority for Health Canada to require submission of a name assessment regarding brand name confusion

• Health Canada invited comments by **September 6, 2013**
Thank You