“Safety” Testing Trademark Candidates for

The Gibbons Institute for Law, Science and Technology, and Seton Hall Law School

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President

Med-ERRS®

ERR on the side of safety℠

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A subsidiary of the Institute for
Safe Medication Practices (ISMP)

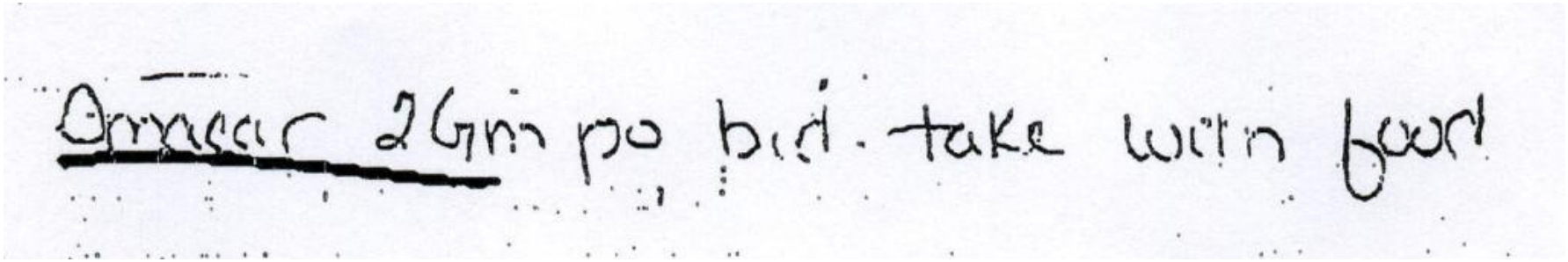
Overview of Talk

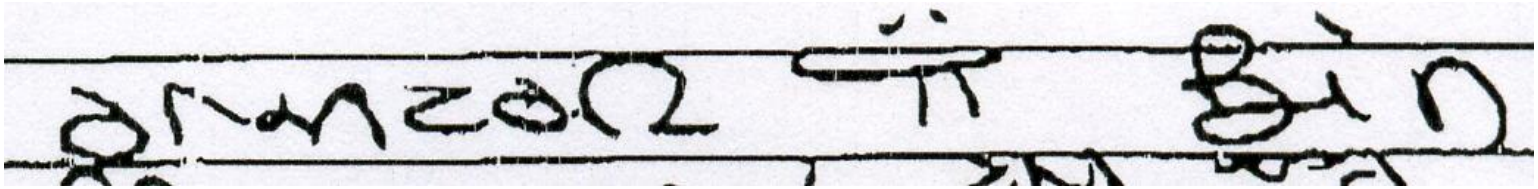
- Why do we do “safety” testing on trademarks?
  - Pharmaceutical trademarks are different
  - Examples of medication errors related to trademarks
- Med-ERRS current process for testing trademarks
- Changes to the regulatory scene
  - US draft guidance
  - Health Canada guidance

Why we safety test pharmaceutical trademarks

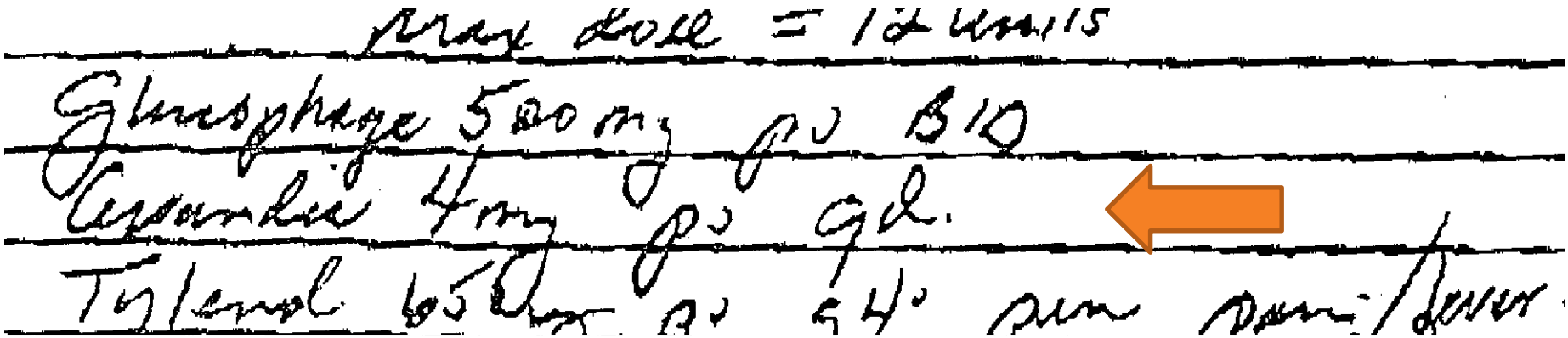
- Added complexity since you need approval of PTO as well as regulatory authorities
- To help prevent medication errors (preventable events) related to name similarity
  - Medication errors occur for many reasons, but some occur due to orthographic and/or phonetic similarity between two trademarks
  - Similarity also can be between two generic (non-proprietary) names, or between one generic name and one trademark.
- To help reduce the risk of regulatory rejection
  - Now becoming “requirement” for review and approval

Amicar or Omacor?

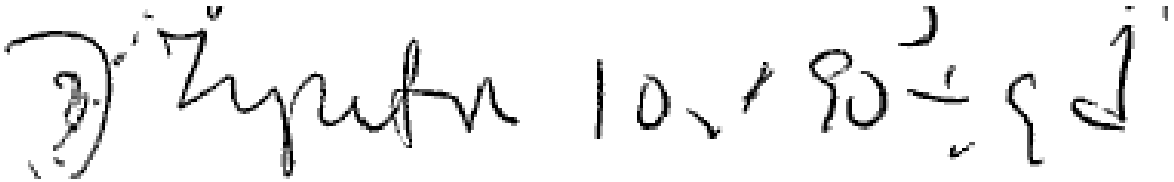




Avandia or Coumadin?



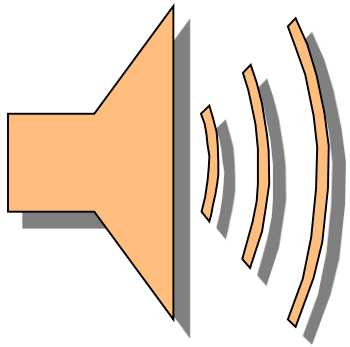
Who would imagine?



How one name can look like another

Similar when spoken

- Evista/Avinza
- Vytorin/Vicodin
- flutamide/thalidomide
- Colazal/Clozaril
- omeprazole/fomepizole
- amantadine/memantine
- Kapidex/Casodex/Capadex



Names within names

RANEXA
T**ranexa**mic acid

ORAP
Orapred

Azor
T**azor**ac

Name Pair Similarity = Metathesis

- Not exactly LA/SA similarity but……
- Metathesis: Transposition within a word of letters, sounds, or syllables, as in the change from Old English "*brid*" to modern English "*bird*" or in the confusion of "*modren*" for "*modern*".
- For former president George Bush = "nuclear" was "nucular"
- Examples of medication name metatheses:
  - Enjuvia/Januvia
  - Cozaar/Zocor
  - Colazal/Clozaril

Problems with Mnemonics

Medication Safety Program
Department of Pharmacy

CAUTION!

Problem: *Medication safety concern regarding* ***similarly named products*** *that have the* ***opposite clinical effect****.*

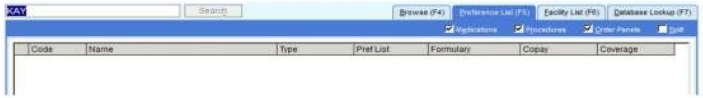
Prescriber types "KAY" *in the computerized order entry screen with the intent of ordering Kayexalate to lower potassium*

The search for KAY returns and selects the 1st alphabetically ordered "KAY" which is KAY CIEL a brand name for a potassium supplement.

Potential Solutions:

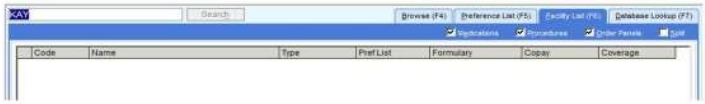
- Warn prescribers of this safety concern – Best Practice Alert
- Adjust setting in CPOE to force a prescriber to choose an item from the search list
- Add Result (potassium) to the order composer
- Add "Kayexalate" to the Facility List for ambulatory prescribing

Personal Preference List *– may or may not show a match.*



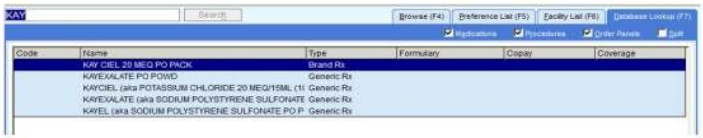
Facility List Search *reveals no match*

Prescriber must switch to ***Database Lookup*** *tab to find a match*



KAY CIEL® *is a brand name (potassium supplement)*

KAYEXALATE® *(to ↓ potassium levels)*



```
BRX410R2              AMC PHARMACY      Drug Utilization Inquiry
                                                Enter Line # ------  ...
Ln Drug# Drug Name                    Strength/Volume          DSFM  Pack Sz
 1 13928 INSULIN-HUMULIN L            100U=1ML                 INJ       10.000
 2 46002 INSULIN-NOVOLIN N            10U=1ML                  INJ       10.000
 3 61501 INSULIN-HUMULIN U            100U=1ML                 INJ       10.000
 4 64042 PINK-INSULIN                 0.06U=1ML                SYRG      25.000
 5 64043 BLUE-INSULIN                 0.5U=1ML                 SYRG      50.000
 6 64044 YELLOW-INSULIN               1U=1ML                   SYRG      50.000
 7 64098 INSULIN-R DILUTED            0.1U=1ML                 VIAL      10.000
 8 97012 INSULIN-REG HUMAN            1U=25ML                  SYRG      25.000
 9 98191 INSULIN-NOVOLIN N            100U=1ML                 INJ       10.000
10 98192 INSULIN-REG HUMAN            100U                     INJ      100.000
11 98664 INSULIN-REG HUMAN            100U                     INJ     1000.000
12 99669 INSULIN-HUMULIN R (FS)       100U                     INJ      100.000
13 99818 INSULIN-HUMAN REG            100U                     INJ      100.000
14 31421 INSULIN NPH INNOLET          1U                       INJ      300.000
15 31321 INSULIN REG INNOLET          1U                       INJ      300.000
16 31721 INSULIN 70/30 INNOLET        1U                       INJ      300.000
17 22203 INSULIN,LANTUS               100U                     INJ       10.000
18 30631 INSULIN,NOVOLIN 70/30        100U                     INJ       10.000
 Enter Line# at top of screen, press ENTER.
F1=Help          F2=Restart       F3=Exit          F4=Prompt
F7=Bkwd          F8=Fwd           F12=Previous     F13=Disp Msg     F14=Send Msg
```

Mnemonics/computer screens

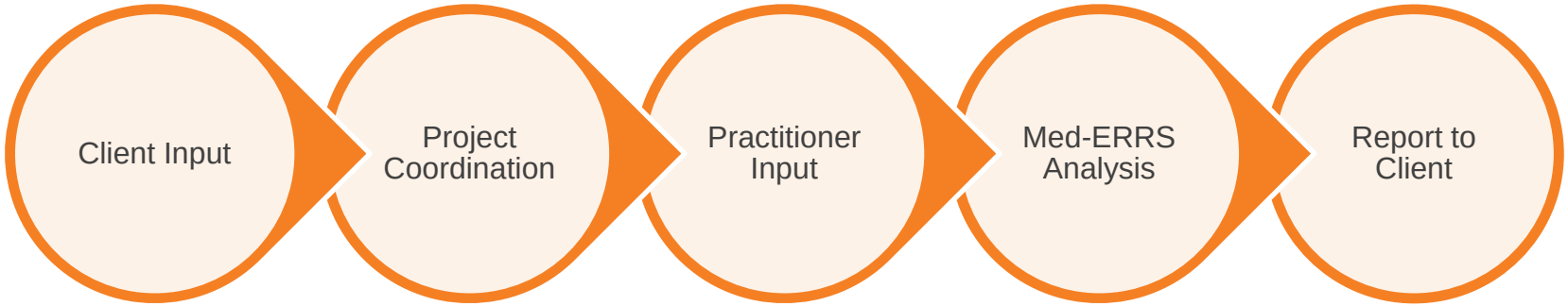
	Mnemonic ↑	Name
1	0034A2U	REG INS/UN MILD -W/OJ AND D50
2	0034AU	REG INS/UNI SLIDING SCALE MILD
3	0034B2U	HUMALOG/UN MILD - W/OJ AND D50
4	0034BU	HUMALOG/UNI SLIDING SCALE MILD
5	0034C2U	REG INS/UNIT MOD -W/OJ AND D50
6	0034CU	REG INS/UNIT SLIDING SCALE MOD
7	0034D2U	HUMALOG/U MODERATE -W/OJ & D50
8	0034DEX	DEXTROSE 50 % FOR SLIDE
9	0034DU	HUMALOG/UNIT SLIDING SCALE MOD
10	0034E2U	REG INS/UNIT AGG - W/OJ & D50
11	0034EU	REG INS/UNIT SLIDING SCALE AGG
12	0034F2U	HUMALOG/UN AGGRESS/OJ AND D50
13	0034FU	HUMALOG/UNIT SLI SCALE AGGRESS
14	0034GLUC	GLUCAGON FOR SLIDING SCALE

ERRS MODEL®

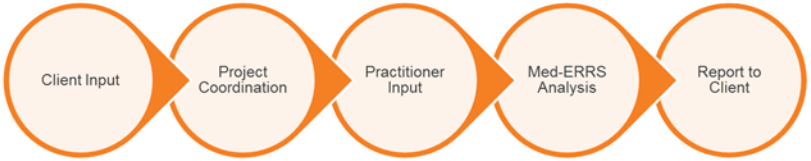
- A pre-marketing approach (typically end of Phase II) that tests for potential look-alike and sound-alike confusion with proposed trademarks

- **Goal of ERRS MODEL:**
  To simulate the drug use process of a client's product to expose potential problem areas so that actions can be taken to minimize or eliminate possible errors

- **5-Step Process:**



Steps 1 & 2: Client Input + Project Coordination



Client Input

- Proposed trademarks are provided by client to Med-ERRS
  - Names should be narrowed down through database searches/preliminary legal clearance
    - Typically ten "finalists" should be chosen for testing
    - Can test up to 30 names
- Clinical information about the product is made available by the client (i.e. indications, dosage, route, etc.
- Expected pronunciation if applicable (syllable breaks, accent marks)
- Trademark information sheet completed by client

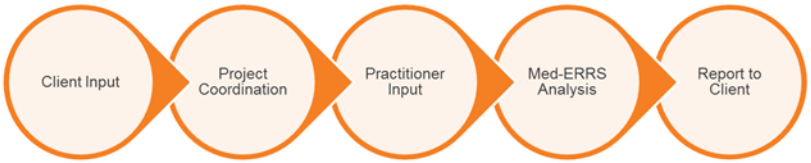
Data Collection

- Client information compiled into data collection tool (survey)
  - Proposed names are scripted
  - Data collection tool sent via e-mail or accessed by participants online through Med-ERRS website
- Participants who complete these surveys are project dependent and are usually either pharmacists or nurses

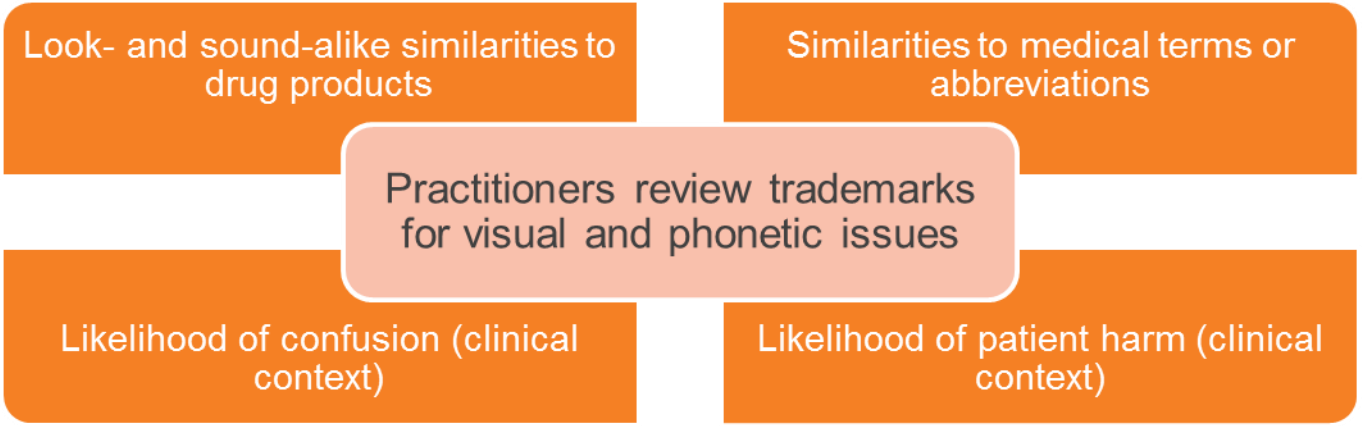
Trademark candidates may be tested in the following countries including:

US	Canada	Specific individual EU countries (e.g., G5)	Various Asian countries (e.g., Japan, India)	South America (Brazil)	Australia

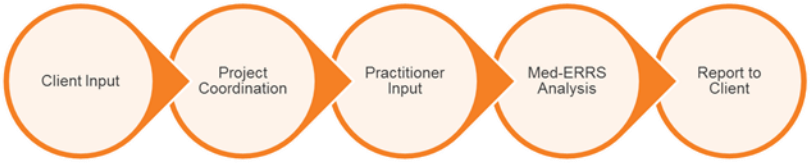
Step 3: Practitioner Input



- Generally utilize 40 – 50 US practitioners and 15 – 20 non-US practitioners
- Self-administered data collection tool takes 20 – 30 minutes for practitioners to complete
  - Completion time depends on the number of names included
- Practitioners complete and submit electronic data collection tool within specified time frame



Step 4: Med-ERRS Analysis

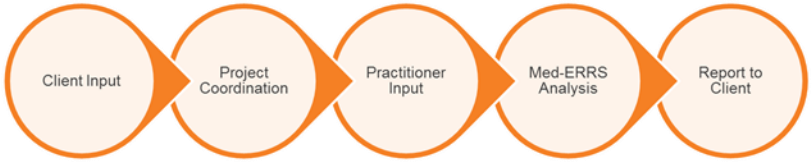


- Collates information from data collection tool
- Med-ERRS expert staff perform comprehensive Failure Mode and Effects Analysis
  - Review of each response submitted by participants and by Med-ERRS professional staff
  - Extensive drug information analysis and follow-up if necessary with country coordinator or participant for clarification
- Trademarks are also evaluated using USAN/INN criteria ("stems")
- Trademark candidates are reviewed for overall concerns for vulnerability (promotional issues)
- For international projects, the requirements of other regulatory authorities (e.g., Health Canada, EMA) must be considered

Goal of FMEA:

- To simulate the environment in which the product will be used in order to bring problem areas to the surface
- To provide actions to minimize or eliminate possible errors, where errors are considered likely

Step 5: Report to Client



- Significant responses that are determined during the FMEA are written into a final report that can be used as part of a regulatory submission
- A vulnerability score is given for each trademark:

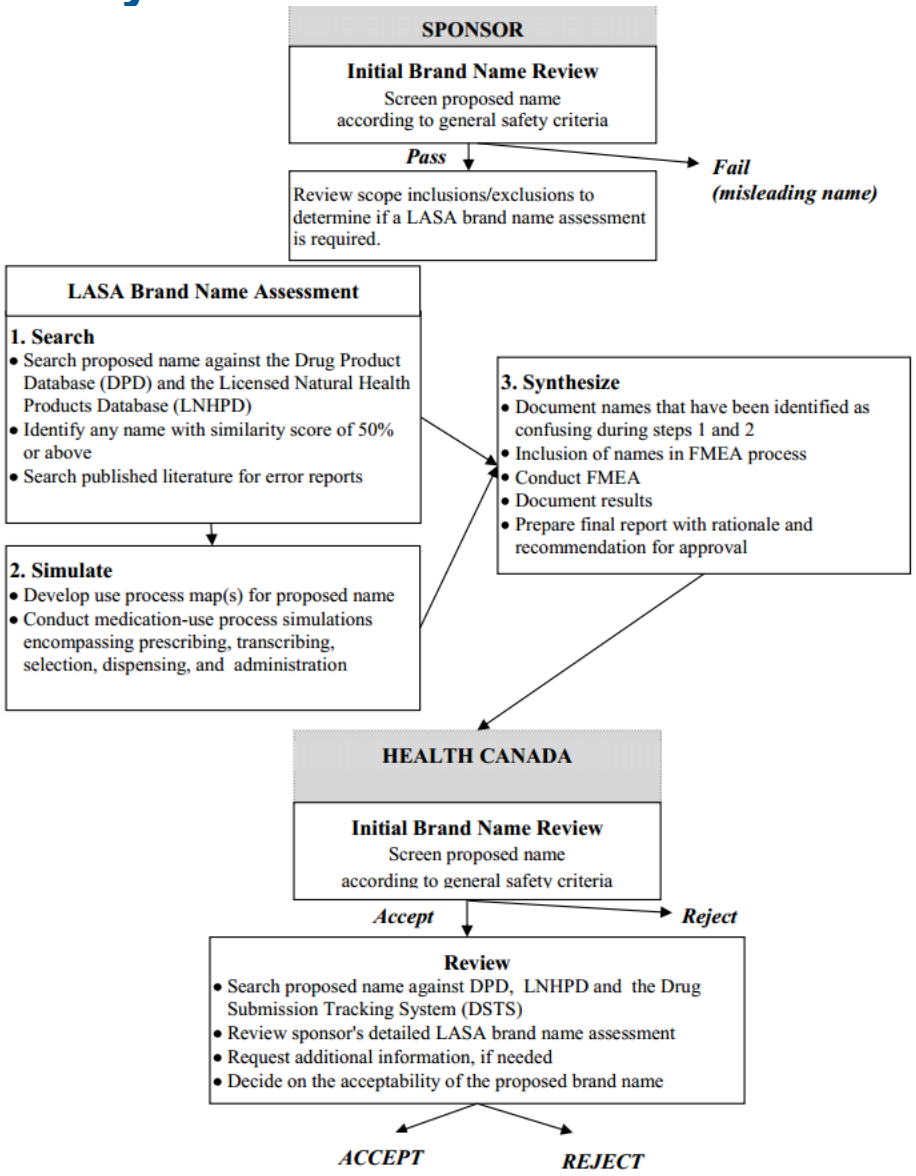
4 - 5 rating (Recommended)	2.5 - 3.5 rating	1 - 2 rating: (Not Recommended)
• **"Low vulnerability"** • Trademarks with a lower risk of confusion and/or patient harm if confused with similar drug names or medical terminology	• **"Moderate vulnerability"** • Trademarks with a moderate risk of confusion and/or patient harm if confused with similar drug names or medical terminology	• **"High vulnerability"** • Trademarks with a high risk of confusion and/or patient harm if confused with similar drug names or medical terminology

- Project Timing
  - Standard US projects completed within 3 weeks
  - Expedited US projects completed within 2 weeks
  - International projects completed within 8 weeks

New guidance, new process

- With the Health Canada guidance in effect as of June 13, 2015, additional steps need to be performed in order to meet those requirements:
  - “Testing of proposed brand names intended to assess likelihood of confusion between proposed name and product names authorized for use in Canada”
  - “Search, Simulate and Synthesize”
- May, 2014: US FDA Draft guidance
  - “…a qualitative systematic framework for evaluating proposed proprietary names before submitting them for FDA review.”

2014 Health Canada Guidance:
"Search, Simulate and Synthesize"



In the future: FDA Draft Guidance

I. Prescreen the Proposed Name

- Obvious similarity in pronunciation or spelling to other names
- Medical/coined abbreviations
- Inert/inactive ingredients
- Combination of active ingredients
- USAN stem
- Same name with different actives
- Reuse of a proprietary name

II. Consider Misleading Nature or Error Potential of Other Nomenclature Attributes

- Inclusion of dosage form, route of administration, manufacturing characteristics, symbols or dosing interval in the name
- Use of modifiers
- Brand name extension
- Dual proprietary name
- Drug names used outside the US
- Rx to OTC switch
- Use of sponsor name in the proprietary name

III. Misbranding Review

- Suggestions that a drug is safer or more effective than has been demonstrated by appropriate scientific evidence
- A fanciful proprietary name may misbrand a product by suggesting that it has some unique effectiveness or composition when it does not

IV. Look-alike Sound-alike (LASA) Safety Review

- Conduct Name Simulation Studies
- Search for similar names using POCA
- Determine similarity scores with other marketed names and categorize as high, moderate, or low similarity
- Use the similarity checklists for the high, moderate, or low similarity to determine whether the name is safe and acceptable from a LASA perspective

Comparisons of US and Canada guidances related to trademarks

Criteria	US	Canada
Number of names submitted/approved	1/1	1/1
What to submit	Components of complete proprietary name submission **(additional studies are optional)**	Proposed name plus brand name assessment
When to submit	Can submit with IND or NDA	N/A
Additional names submitted?	Yes, but will only review if first name found unacceptable, and sponsor must withdraw first name	Yes
Use of qualifiers/modifiers	Recommended to use established modifier that has not been a source of confusion	May be acceptable if meets criteria
Testing methodology	Specified in guidance (prescreening questions, POCA, simulation studies) (**recommended**)	Specified in guidance ("search, simulate, synthesize") (**required**)
What will be tested	Prescription and over-the-counter products	Prescription products only
Number of error scenarios for simulation testing	Minimum of 20 scenarios, including consumers for OTC drugs	At least 5 simulations and 100 practitioners, some of which speak French (20-25%)

Comparisons of US and Canada guidances related to trademarks

Criteria	US	Canada
Approval by other regulatory authorities	N/A	Sponsor may submit assessment that was sent to other regulatory authorities
Reasons for rejection	Confusability/promotional issues (misbranding)	Confusability/misleading
Use of INN/USAN stems	USAN stems not accepted in stem position	INN/USAN not allowed in trademark in stem position
Use of revoked/withdrawn names	Generally not accepted	Raises “red flag”
Language	English	English/French
Testing by regulatory authority	Yes	No – Will use sponsor’s review
Use of same or similar trademark from other country for different product	Generally not accepted	N/A
Searching tool criteria	POCA combined score >70% don't use, >50% evaluate, less than 50% probably ok	POCA combined score or another tool can be used, 50% or greater must review
Databases to search	RxNorm and Drugs@FDA for POCA	DPD, LNHPD

Thank you!

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