Best Practices for Proprietary Name Design

Danielle Harris, PharmD, Deputy Director
Division of Medication Error Prevention and Analysis (DMEPA)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
CDER | US FDA

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Learning Objectives

- Understand what contributes to medication errors due to proprietary name confusion
- Understand the purpose of the draft Guidance for Industry: *Best Practices in Developing Proprietary Names for Drugs*
- Understand FDA's current thinking on how to develop proprietary names that do not cause or contribute to medication errors or violations of the FD&C Act
- Understand FDA's process for reviewing proposed proprietary names

Proprietary Name Guidance and MAPPs

Guidance documents:

1. Final Guidance for Industry: Contents of a Complete Submission for the Evaluation of Proprietary Names
2. Draft Guidance for Industry: Best Practices in Developing Proprietary Names for Drugs

Manual of Policies and Procedures (MAPPs):

1. MAPP 6720.2: Procedures for Handling Requests for Proprietary Name Review
2. MAPP 6720.4: Procedures for Sharing Non-public Information on Pending Proposed Proprietary Names

FDA Draft Guidance for Industry…

Best Practices in Developing Proprietary Names for Drugs

Purpose

- To help minimize proprietary name-related medication errors and avoid adoption of proprietary names that contribute to violations of the FD&C Act
- To describe the framework FDA uses in evaluating proposed proprietary names that is also available to sponsors to use before submitting names for FDA review

Contents

- Prescreening for error-prone attributes
- Additional best practices for proprietary name design
- Misbranding review
- Methods for evaluating similarity of a proposed name to other names
  - Name simulation studies
  - FDA Phonetic and Orthographic Computer Analysis (POCA)

Proprietary Name Confusion…

Contributing Factors

Environmental & Human Factors

- Stressful work environment
- Frequent interruptions & distractions
- Poor lighting
- Noise level

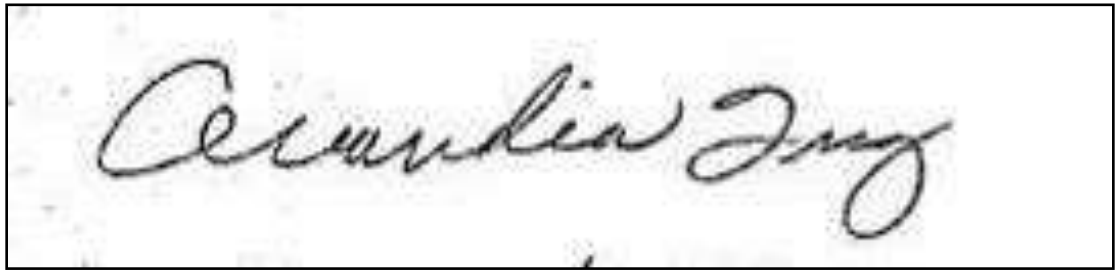
Confirmation Bias

Aoccdrnig to rscheearch at Cmabrigde Uinervtisy, it deosn't mttaer in waht oredr the ltteers in a wrod are, the olny iprmoetnt tihng is taht the frist and lsat ltteer be at the rghit pclae. The rset can be a toatl mses and you can sitll raed it wouthit a porbelm.

Tihs is bcuseae the huamn mnid deos not raed ervey lteter by istlef, but the wrod as a wlohe.

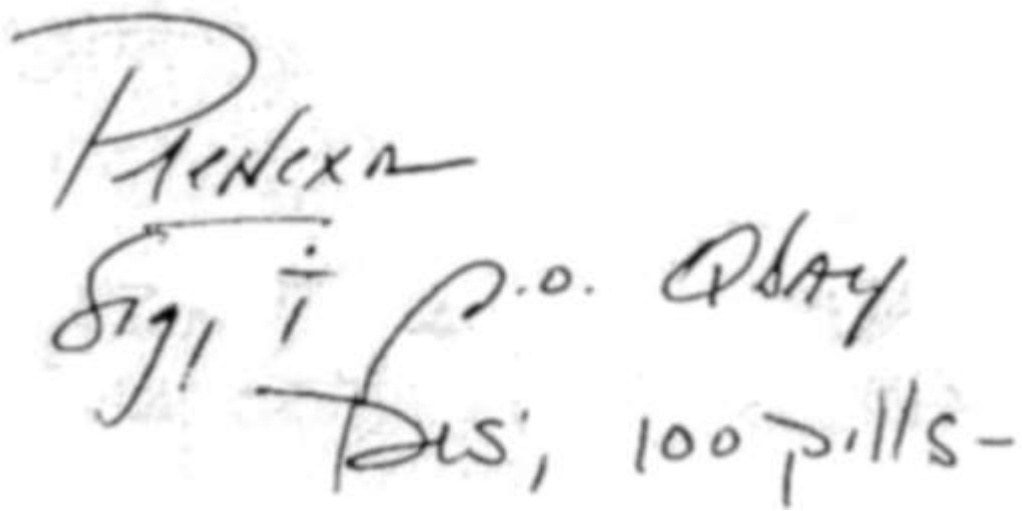
Amzanig huh?

Handwriting Legibility



The drug was supposed to be Avandia. The doctor did not close the "A" at the top so the pharmacist thought it was a "C" and filled it with Coumadin. The patient was dispensed Coumadin and nearly bled to death. His entire large intestine had to be removed.

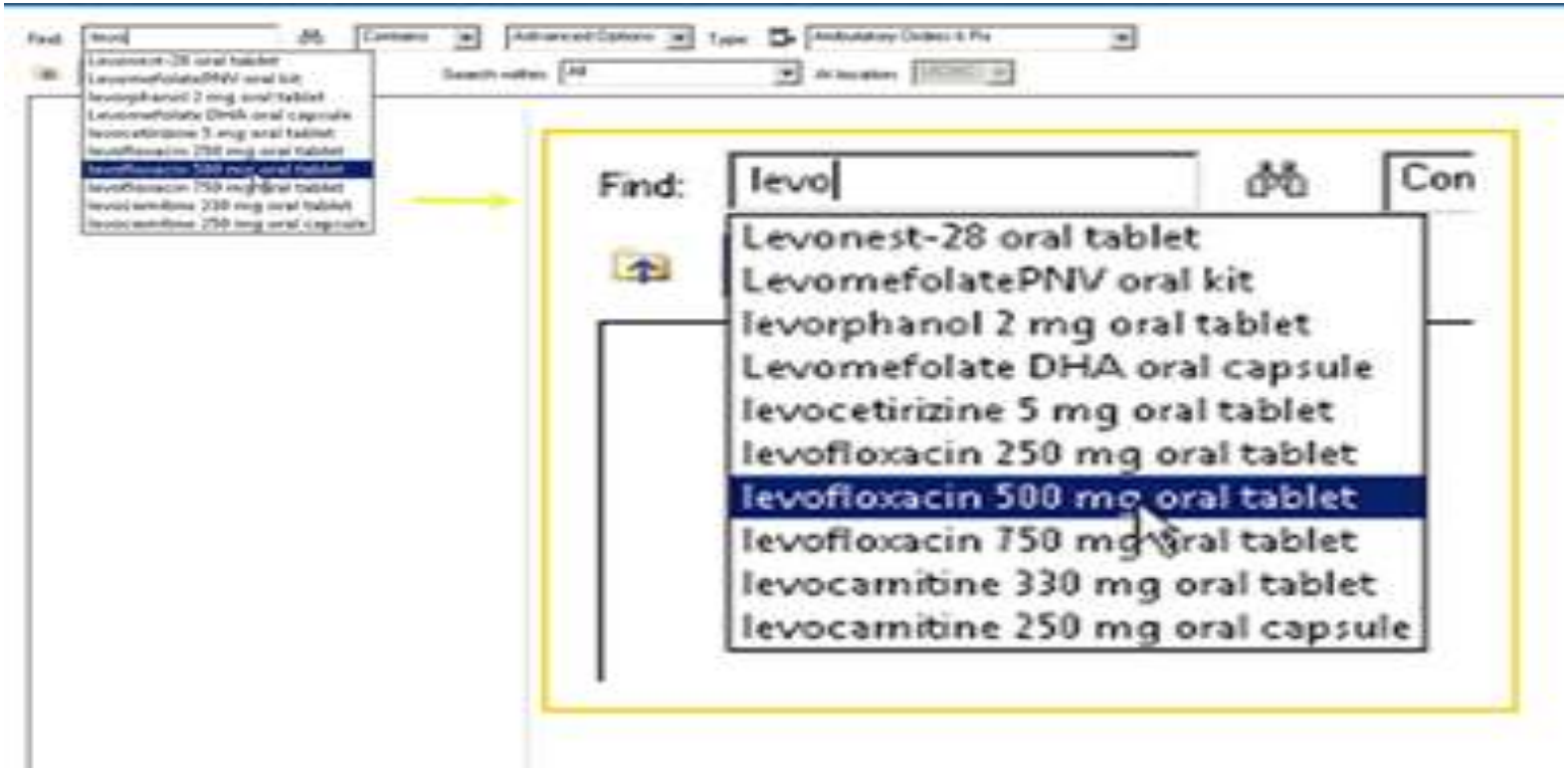
Look-alike Sound-alike (LASA) Names



Ranexa or Prenexa?

Institute for Safe Medication Practices.Safety briefs.
ISMP Med Saf Alert Community/Ambulatory Care. 2012;11(3):1-4.

Role of Electronic Prescribing



FDA Draft Guidance for Industry…

Prescreening for Error-prone Attributes

Obvious Similarity to Other Names

- FDA considers a proposed proprietary name to be misleading if it may be confused with the proprietary name or the established name of a different drug or ingredient because of similar spelling or pronunciation (21 CFR 201.10(c)(5)).

Sbiatev vs Sbiotec

Inert or Inactive Ingredients

Proprietary names should not incorporate any reference to an inert or inactive ingredient (21 CFR 201.10(c)(4)).

Combinations of Active Ingredients

Proprietary names of fixed combination drug products should not include or suggest the name of one or more, but not all, of its active ingredients (see 21 CFR 201.6(b)).

Reusing a Proprietary Name

- Do not reuse a proprietary name of a discontinued product for different drug or biological product
- Proprietary names are used in prescribing for an extended period of time even after product discontinuation[1] and in some cases this has lead to name confusion errors
- There is a strong risk that users may continue to associate the name with the original discontinued product

1. Tu, CM, K Taylor, and G Chai. Use of proprietary names by prescribers for discontinued brand drug products with existing generic equivalents, Drug Information Journal (published online August 21, 2012), available at http://dij.sagepub.com/content/early/2012/08/21/0092861512456282.full.pdf+html, last accessed 12/10/19

United States Adopted Name (USAN) Stems

- USAN stems are intended to indicate a pharmacological or chemical trait of a drug, and a single stem may be applicable to multiple drug products

- Proprietary names should not incorporate USAN stems in the position that USAN designates for the stem (e.g., Drugo***statin***) as this can result in the creation of multiple similar proprietary names and/or proprietary names that are similar to established names

- FDA will no longer object to the inclusion of two-letter stems

(-ac, -aj-, ef-, -fo-, io-, -io-)

Brand Name Extension

- Sponsors should not use a proprietary name that is already associated with one or more marketed drug products for a product that *does not share at lease one active ingredient(s) or active moiety(ies)* with the marketed product(s)
- Health care professionals familiar with an existing product may, in some cases, equate that product's proprietary name with the product's active ingredients (or active moieties) or uses

  Sbiatin (ibuprofen)

  Sbiatin PM (acetaminophen and diphenhydramine)

FDA Draft Guidance for Industry…

Additional Best Practices for Proprietary Name Design

Inclusion of Medical Abbreviations

- Sponsors should avoid using symbols, dose designations, and medical abbreviations in the proprietary name in a manner which could be misleading or lead to error

- A list of potentially confusing abbreviation and symbols can be found in The Joint Commission's "Do Not Use" list or the Institute for Safe Medication Practices (ISMP) List of Error-Prone Abbreviations, Symbols, and Dose Designations

Namepo

Inclusion of Product-Specific Attributes

- For flexibility in future product development, FDA recommends sponsors avoid incorporating product-specific attributes in the name
  - manufacturing characteristics (e.g., “NameLyophilized”)
  - dosage form (e.g.. “Nametabs”)
  - route of administration (e.g., “Nameoral”)
- When used, should be consistent with the product and not pose risk of medication error
- Sponsor may wish to consider future changes (new dosing intervals, formulations, dosage forms, indications, and patient populations, etc.) may render the original proprietary name inaccurate

Incorporation of Sponsor's Name

- Proprietary names should not incorporate the sponsor's name, or some part of the sponsor's name across multiple products
- This practice results in creating multiple similar proprietary names, increasing the risk of confusion across products

ABCName1

ABCName2

ABCName3

Modifiers as Components of Proprietary Name

- Some proprietary names are constructed of a root proprietary name modified by added words or components, which are referred to as **modifiers**.
- Used to distinguish among multiple products that contain at least one shared active ingredient
- Modifiers may be used to convey;
  - Distinguishing product characteristics (e.g., Name ODT, Name XR)
  - Delivery Device component (e.g., Drugname Pen)
  - Some other aspect of the product (e.g. indication, formulation etc.)

Modifiers as Components of Proprietary Name

- Inconsistencies in the use of modifiers and the absence of a standardized meaning for some modifiers have been a source of confusion to end users
- Confusion stemming from the use of modifiers has led to medication errors, such as dispensing and administering wrong formulation, wrong dose, wrong strength, or wrong frequency
- Medication errors have also occurred within the same product line if the distinguishing modifier is omitted or disregarded when a product is prescribed or dispensed.

Considerations When Selecting a Modifier

- Is there a **need** for modifier?
- Does the modifier convey **accurate information** about the product?
- Does the modifier **effectively differentiate** the product from other products in the product line?
- What is the intended **meaning**? Do you have **data to support** end users understand this meaning?
- What is your **rationale for the placement** in relation to the root proprietary name?
- What is the risk associated with modifier **misinterpretation** or **omission**?
- Is the modifier **currently used** in the marketplace?

Existing Modifiers

FDA encourages sponsors to select, whenever possible, an existing modifier with an established meaning that has not been a source of confusion

Modifier	Commonly Understood Meaning
XR	Extended-release product
ER	Extended-release product
DS	Double strength
LA	Long acting
Pak	For example, dose card package or carton containing two or more drugs
Depot	Depot injection
ODT	Orally disintegrating tablets
Lo	Used as a modifier before the root name in oral contraceptives to indicate low-dose estrogen
Tri	Used as a modifier before the root name in oral contraceptives to indicate triphasic
Fe	Used to indicate ferrous component

Existing Modifiers

FDA encourages sponsors to select, whenever possible, an existing modifier with an established meaning that has not been a source of confusion

Modifiers	Commonly Understood Meaning
Allergy	For treatment of allergy symptoms
D	Contains a decongestant
PM	For nighttime use
DM	Contains dextromethorphan
For Men	For use only in men
For Women	For use only in women
12h	Dosed every 12 hours
24h	Dosed every 24 hours

Prescription to Nonprescription Switch "Rx-to-OTC" Switch

- FDA evaluates on a case-by-case basis when drug product is "switched" from prescription to OTC status
- Full switch to OTC → **all** indications, dosage forms, strengths, etc. are switched
  - May consider use of the original name, a modified form of the original name, or novel name
- Partial switch to OTC → **some** indications, dosage forms, or strengths are switched
  - May consider modified form of original name or a novel name

Challenge Question #1

Which of the following proposed proprietary names is likely to generate an objection from FDA:

A. Sbiat**iv** for an intravenous product

B. Sbia**statin** for a cholesterol lowering product

C. Posbia for an oral tablet

D. Sbialar **ODT** for an orally disintegrating tablet

FDA Draft Guidance for Industry…

Review for misbranding and other legal concerns

Misbranding Review

- Sponsors should avoid using a proprietary name that could contribute to any violation of the FD&C Act, for example, a drug is misbranded if its labeling is false or misleading in any particular (section 502(a)).
- 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

Curesbia

FDA Draft Guidance for Industry…

Methods for evaluating similarity of a proposed name to other names

Look-alike Sound-alike (LASA) Safety Assessment

Consider phonetic, spelling, and orthographic similarity

Conduct name simulation studies (NSS)

Search for similar names using FDA's Phonetic and Orthographic Computer Analysis (POCA) program

- Determine similarity scores with other marketed names
- Categorize as high, moderate, or low similarity based on match score

Use checklists for high, moderate, or low similarity pairs to help determine whether the name is safe from a LASA perspective

Name Simulation Studies

- Intended to test how subjects respond to a proposed proprietary name by asking them to use the name in simulated real-world use conditions
- The more closely and fully the simulation approximates real-world use conditions, the more generalizable the results
- Name simulation tasks should reflect the full range and variety of tasks involved in the selecting, purchasing, prescribing, transcribing, dispensing, and administering of drugs
- Results should be analyzed carefully to identify potential errors

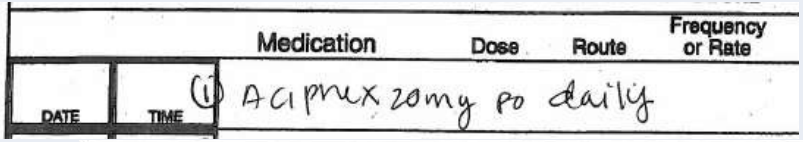
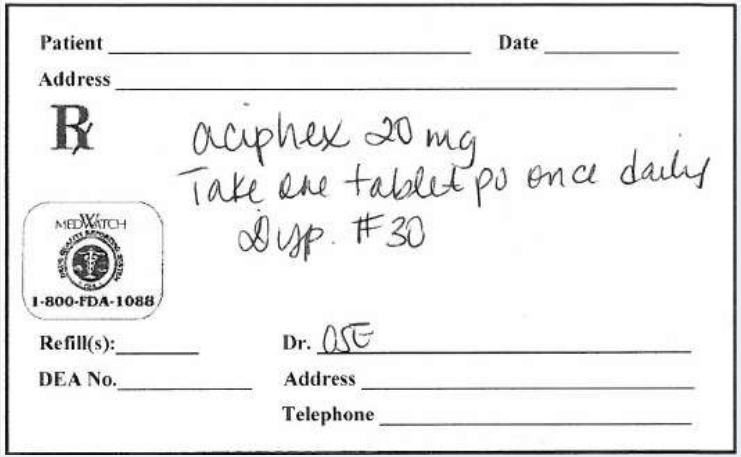
Name Simulation Studies

- *FDA RX Studies System* – FDA's prescription simulation program designed in 2003 to test for potential confusion of proposed proprietary names with marketed or pending drug names
  - Since 2003 FDA has conducted studies with written (inpatient and outpatient) and verbal simulated prescriptions
- As the use of electronic prescribing, or computerized provider order entry (CPOE) increases, FDA recognizes the need to test for potential errors related to drug name displays

Name Simulation Studies

- A CPOE prescription simulation module was implemented in late 2019
- Developed to provide a drug name display and user interface that is not specific to any particular CPOE system
- Intended to test for name confusion between the proposed proprietary name and drug names that may appear in the dropdown list during order entry in an electronic prescribing scenario
- Uses the same data sources currently found in the FDA POCA system to provide CPOE pick lists

Prescription Simulation: Aciphex

Handwritten Medication Order/Prescription	Verbal Prescription
Medication Order: 	Aciphex 20 mg. Take one tablet by mouth once daily. Dispense: 30
Outpatient Prescription: 	
CPOE Study Sample (Font: sans-serif, 12 point, bold)	
Aciphex	

Prescription Simulation: Aciphex

Study Name: Aciphex

Total	**19**	**33**	**19**	**20**	
INTERPRETATION	**OUTPATIENT**	**CPOE**	**VOICE**	**INPATIENT**	**TOTAL**
ACIFEX	0	0	1	0	1
ACIPHEN	1	0	0	0	1
ACIPHEX	18	33	17	17	85
ACIPNEX	0	0	0	1	1
ACIPREX	0	0	0	2	2
ASAFEX	0	0	1	0	1

Phonetic and Orthographic Computer Analysis

- The Phonetic and Orthographic Computer Analysis (POCA) program is a software tool that uses an advanced algorithm to determine the orthographic and phonetic similarity between two drug names
- First released to public in Spring 2009*; available for download → POCA
- FDA uses POCA to compare a drug name against multiple drug names contained in both internal* and external data sources. Publicly available data sources in the most recent version are:
  - DrugsAtFDA (updated monthly)
  - RxNorm (updated monthly)
  - Suffixes in the proper name of approved biological products (updated monthly)
  - United States Adopted Names (USAN)

**proposed proprietary name listings are only available to FDA - not the public*

Phonetic and Orthographic Computer Analysis

- POCA is a central component of FDA's safety review
- Search provides three data sets: COMBINED orthographic and phonetic matches, phonetic matches, and orthographic matches
- The COMBINED measure of similarity has been positively correlated to errors involving name confusion
- Higher scores equate with greater similarity
- FDA continues to work on improving system performance

POCA Database Updates

- December 2016 - Algorithm Changes to Orthographic Component
- The revised algorithm is designed to better capture the shift in the type of errors that are being reported due to using electronic prescribing
- Revised to put more emphasis on:
  - similarity that occurs at the beginning of the word
  - on exact letter matches
  - on consecutive and non-consecutive shared letters

POCA Database Updates

- Revised to give the same orthographic similarity score if candidate and source names are switched (bidirectional)

- To accommodate for the increased sensitivity of the revised algorithm, FDA has revised the scores associated with low and moderate similarity:
  - Highly Similar Pair: combined score ≥70%
  - Moderately Similar Pair: combined score ≥55% (previously ≥50%) to ≤ 69%
  - Low Similarity: combined score ≤54% (previously <49%)

FDA Draft Guidance for Industry…

Evaluating the Results – Safety Determination of Similar Names

Evaluating Similar Name Pairs

- The POCA search will provide three data sets: (1) COMBINED orthographic and phonetic matches, (2) phonetic matches, and (3) orthographic matches.
- Review the COMBINED orthographic and phonetic matches and group the name pairs into one of the following three categories:
  - Highly Similar Name Pair: combined score ≥70%
  - Moderately Similar Name Pair: combined score ≥55% to ≤ 69%
  - Low Similarity Name Pair: combined score ≤54%

Analyzing the Results

- Checklists are provided in the Guidance for each similarity category using the principles of Failure Mode and Effects Analysis
- The checklists are intended to increase the transparency and predictability of the safety determination of whether a proposed proprietary name is vulnerable to confusion from a look-alike or sound-alike perspective

Highly Similar Names (>70%)

- Differences in product characteristics may not prevent the risk of a medication error
- Checklist focuses on first whether the names themselves have sufficient differences in appearance and sound to avoid to confusion
- If names are viewed as sufficiently different, then consider the influence of product characteristics on the potential for confusion (i.e. Consult the moderately similar checklist)

Moderately Similar Names (≥55% to ≤ 69%)

- Focus is attributes that are known to cause confusion
- Name pairs that have overlapping or similar strengths or doses have a higher potential for confusion
  - Evaluate these pairs further to determine if the pattern of orthographic or phonetic differences in the names would prevent confusion

Low Similarity Names (≤54%)

- In most circumstances, these names are viewed as sufficiently different to minimize confusion.
- Exceptions might occur where there are data from simulation studies that suggest that the name is susceptible to misinterpretation as marketed product name.

Role of Product Characteristics

- Product strength and dose is an important consideration
  - For similar names, the risk of medication error is potentiated when the strengths and doses overlap or are similar to one another.
  - However, if none of the strengths overlapped, the name similarity ***might*** not lead to errors.
- Consider: Intuniv and Invega
  - 3 mg strengths **have** been confused
  - Intuniv 1 mg, 2 mg, and 4 mg and Invega 1.5 mg, 6 mg, and 9 mg product strengths **have not** been confused.

Role of Product Characteristics

- **If two products have highly similar names, differences in the product profile may not reduce the risk of error**

- Confusion has occurred when doses, therapeutic uses, dosage forms, route of administration, and setting of use are different
  - Cerebyx (an injectable anti-convulsant drug) and Celebrex (an oral NSAID)
  - Advair (an inhalation product) and Advicor (a tablet)
  - Durasal (a topical wart remover) and Durezol (an ophthalmic drop)

Final Determination on Name Acceptability

- The acceptability of a proposed proprietary name is based on FDA's review of all information and analyses described in the guidance along with any information submitted by the Applicant
- FDA may reject a name if, based on the information provided or in its own review, it determines the name:
  - causes confusion with other products that can result in medication errors and preventable harm or
  - is misleading with respect to the therapeutic effectiveness, composition, or the safety of the product.

Challenge Question #2

Which is likely to potentiate the risk for name confusion in moderately similar names?

A. Same frequency of administration

B. Same strength and dose

C. Same route of administration

D. Same indication of use

Questions?

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Resources

- Draft Guidance: Best Practices in Developing Proprietary Names for Drugs
- Guidance: Contents of a Complete Submission for the Evaluation of Proprietary Names
- MAPP 6720.2, Rev. 1, Procedures for Handling Requests for Proprietary Name Review.
- MAPP 6720.4- Procedures for Sharing Non-public Information on Pending Proposed Proprietary Names
- Proprietary Name Review Concept paper (PILOT PROGRAM)


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