Guidance for Industry

Best Practices in Developing Proprietary Names for Drugs

DRAFT GUIDANCE

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For questions regarding this draft document contact (CDER) Office of Surveillance and Epidemiology, Division of Medication Error Prevention and Analysis, Kellie Taylor at 301-796-0157, or (CBER) Office of Communications, Outreach and Development at 800-835-4709 or 240-402-7800.

U.S. Department of Health and Human Services
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Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

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Drug Safety

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Office of Communications, Division of Drug Information,
Center for Drug Evaluation and Research
Food and Drug Administration
10903 New Hampshire Ave., WO51, Room 2201
Silver Spring, MD 20993-0002
Tel: 301-796-3400; Fax: 301-847-8714; E-mail: druginfo@fda.hhs.gov
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Center for Biologics Evaluation and Research
Food and Drug Administration
10903 New Hampshire Ave., WO71, Room 3128
Silver Spring, MD 20993
Phone: 800-835-4709 or 240-402-7800
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U.S. Department of Health and Human Services
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Center for Drug Evaluation and Research
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Best Practices in Developing Proprietary Names for Drugs

This draft guidance, when finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

I. INTRODUCTION

FDA is issuing this guidance to help sponsors of human drugs, including those that are biological products, develop **proprietary names**[2] that do not cause or contribute to medication errors[3] or otherwise contribute to the misbranding of the drug. This guidance describes design practices to help avoid such errors with proprietary names and provides a qualitative systematic framework for evaluating proposed proprietary names before submitting them for FDA review. This guidance does not address the selection of **established names** or **proper names**.

This guidance applies to all human prescription and nonprescription drug products, including those that are biological products. In this guidance, all such products are jointly referred to as *products*, and persons responsible for developing the products are referred to as *sponsors*.

This is the last in a series of three guidance documents that FDA is issuing to help sponsors minimize the potential for medication errors when designing and developing products. The first guidance focuses on minimizing risks associated with the design of the drug product and its

[1] This guidance was prepared by the Division of Medication Error Prevention and Analysis and the Division of Professional Drug Promotion in the Center for Drug Evaluation and Research (CDER), and the Advertising and Promotional Labeling Branch in the Center for Biologics Evaluation and Research (CBER) at the Food and Drug Administration.

[2] Terms that appear in bold type upon first use are defined in the Glossary.

[3] As used in this guidance, a *medication error* is any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the healthcare professional, patient, or consumer (National Coordinating Council for Medication Error Reporting and Prevention, http://www.nccmerp.org/aboutMedErrors.html).

container closure system.[4] The second guidance focuses on safety aspects of the container **label** and carton **labeling** design.[5] This third guidance presents FDA's current thinking on best practices for developing and selecting proposed proprietary names.[6]

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidance documents describe FDA's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in FDA's guidance means that something is suggested or recommended, but not required.

II. BACKGROUND

Selecting a proprietary name is a critical element in the design and development of drug products because **end users** may rely, in part, on the proprietary name to identify which product, among thousands of available products, is intended for or used by a given patient. For this reason, accurate interpretation by the end user is essential. If end users cannot readily distinguish among proprietary names that are similar phonetically (sound-alike names) or in their spelling or orthographic appearance (look-alike names), or are otherwise confusing or misleading, the patient might receive the wrong product or it might not be possible to correctly identify the product used.

A report released in 1999 by the Institute of Medicine (IOM) described medication errors as a significant public health concern that accounts for an estimated 7,000 deaths annually in the United States.[7] The report recommended that FDA encourage pharmaceutical companies to test proposed proprietary names to identify and remedy potential sound-alike and look-alike

[4] See the FDA draft guidance for industry *Safety Considerations for Product Design to Minimize Medication Errors* (December 2012). When final, this guidance will represent FDA's current thinking on this topic. The guidances referenced in this document are available on the FDA Drugs guidance Web page at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm. We update guidances periodically. For the most recent version of a guidance, check the FDA Drugs guidance Web page.

[5] See the FDA draft guidance for industry *Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors* (April 2013). When final, this guidance will represent FDA's current thinking on this topic.

[6] This third guidance on best practices for developing and selecting proprietary names is intended to complement our existing guidance for industry *Contents of a Complete Submission for the Evaluation of Proprietary Names.* That guidance represents FDA's current thinking on the information that should be submitted to commence FDA evaluation of proposed proprietary names, as well as the timelines and processes for review.

[7] Kohn LT, Corrigan JM, Donaldson MS, eds. *To Err Is Human: Building a Safer Health System*. Institute of Medicine, National Academies Press: Washington, DC, 2000 (contains nonbinding recommendations). See also Phillips DP, Christenfeld N, and Glynn LM. Increase in US medication-error deaths between 1983 and 1993. The Lancet. 351:643-644, 1998.

confusion with existing drug names.[8] In July 2006, the IOM published a follow-up report titled *Preventing Medication Errors* (IOM 2006), which emphasized in part that proprietary name design should focus on end users' needs and understanding, and urged FDA to apply the principles of cognitive and human factors engineering to the selection and evaluation of proprietary names.[9,10]

As FDA has long recognized, and addressed on numerous occasions in recent decades, confusion over proprietary names can cause or contribute to significant medication errors. Our primary focus has been to develop and communicate to sponsors a systematic, standardized, and transparent approach to proprietary name evaluation within the product review and approval process. As part of this initiative, FDA held public meetings in June and December of 2003 to discuss the methods used for proprietary name evaluation. In 2007, FDA formally committed to certain performance goals, including implementing evaluation measures to help reduce medication errors related to look-alike and sound-alike proprietary names (PDUFA IV performance goals).[11] In 2008, the Agency held another public meeting, to further discuss testing and evaluating proprietary names, and initiated a pilot project on proprietary name review.[12] The 2008 meeting focused on (1) advances and current limitations in the science of proprietary name evaluation, (2) FDA's recommendations for best practices in the absence of a "gold standard," and (3) details of the proposed pilot project. All the evaluation methods proposed by FDA were judged by the participating expert panel to be complementary and of value in the proprietary name testing process.

This guidance, which we are issuing in partial fulfillment of the PDUFA IV performance goals, presents FDA's current thinking on best practices for developing and selecting proposed proprietary names.[13] Appendix B provides a figure that outlines the considerations for developing and selecting a proposed proprietary name. These considerations are further described in further detail in sections III, IV, and V of this guidance:

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[8] IOM 2000, *To Err Is Human*. Chapter 7, Recommendation 3, p. 136. The IOM recommendations were consistent with an earlier FDA report that likewise underscored the importance of reducing errors from proprietary name confusion. HHS/FDA Report to FDA Commissioner from the Task Force on Risk Management titled, *Managing the Risks From Medical Product Use* (May 10, 1999).

[9] IOM, *Preventing Medication Errors*. Chapter 6, Recommendation 4, p. 280.

[10] IOM, *Preventing Medication Errors.* Chapter 6, Actions to Improve Drug Naming, Labeling, and Packaging, pp. 281-282.

[11] These performance goals and commitments were undertaken in connection with the reauthorization and expansion of the Prescription Drug User Fee Act (PDUFA IV reauthorization), which was signed into law on September 27, 2007, as part of the Food and Drug Administration Amendments Act of 2007 (FDAAA) (Public Law 110-85). For more information on FDA's PDUFA IV performance goals, see FDA's Web site at http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm119243.htm.

[12] For further information, including a summary of the public meetings held in June 2003, December 2003, and June 2008, see FDA's *PDUFA Pilot Project Proprietary Name Review Concept Paper* (2008 Final Concept Paper) at 4-5, available at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.

[13] See 2008 Final Concept Paper at 5.

- Sections III and IV focus on evaluating the safety concerns within the name or related to the naming strategy.
  - — Section III describes our recommended prescreening for proposed proprietary names; and the focus of this section is to provide our current thinking on readily identifiable aspects of the name that are very likely to raise concern for FDA.
  - — Section IV describes additional attributes related to the proposed name or naming strategy that may or may not raise a concern for FDA, and such attributes should be considered on a case-by-case basis.
- Section V describes our current thinking on evaluating the proposed names for look-alike and sound-alike risks as well as our recommendations for evaluating the proposed name to identify any concerns that may arise related to misbranding.

III. RECOMMENDATIONS FOR PRESCREENING PROPRIETARY NAME CANDIDATES

FDA's objections to proposed proprietary names are often for readily identifiable reasons. This section identifies practices that have led to names that FDA found objectionable and thus should be avoided by sponsors. We recommend that sponsors screen proposed proprietary name candidates for the characteristics described below as a first step before proceeding with a full assessment of safety and misbranding concerns and, when applicable, submission for FDA review. Proposed proprietary names that fail this preliminary screening are unlikely to be viable candidates for FDA acceptance. A checklist is provided in Appendix C to aid in the prescreening of the names, and the text below explains FDA's thinking with respect to each of these aspects.

A. Obvious Similarities in Spelling and Pronunciation of Proprietary Names

Generally, proprietary names should not be similar in spelling or pronunciation to proprietary names, established names, or ingredients of other products. FDA may consider 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 (see 21 CFR 201.10(c)(5)). We recommend that sponsors conduct a preliminary screening to eliminate names with obvious similarities to the names of existing products known to the sponsor. Later in the process, a full assessment of safety and misbranding concerns will need to be performed to identify less obvious but still confusing similarities, as described in section V.B.

B. Medical Abbreviations

Proprietary names should not incorporate medical abbreviations (e.g., QD, BID) or others commonly used for prescription communication because the incorporation of such abbreviations could inadvertently be a source of error. In particular, sponsors should avoid using abbreviations, symbols, and dose designations that have been identified as potentially confusing

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.[14,15]

C. Inert or Inactive Ingredients

Proprietary names should not incorporate any reference to an inert or inactive ingredient in a way that creates an impression that the ingredient's value is greater than its true functional role in the formulation (see 21 CFR 201.10(c)(4)).

D. 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)). Such names can mislead the end user by implying that the product contains only the ingredient(s) included in the name. (Section 201(n) of the Federal Food, Drug, and Cosmetic Act (FD&C Act); 21 U.S.C. 321(n).)

E. United States Adopted Name (USAN) Stems

Proprietary names should not incorporate United States Adopted Name (USAN) stems in the position that USAN designates for the stem. USAN stems are intended to indicate a pharmacological or chemical trait of a drug, and a single stem will be applicable to multiple drug products. Use of these stems in the position designated by USAN within the proprietary names, even when such use is consistent with the USAN meaning, can result in the creation of multiple similar proprietary names and/or proprietary names that are similar to established names, leading to an increased risk of medication errors because of name confusion. Sponsors should screen proposed proprietary names against the stem list created by the USAN Council to ensure a USAN stem is not present in the stem position in the proprietary name.[16] In rare circumstances, it might be acceptable to include a USAN stem in the USAN-designated position within the proposed proprietary name. Such circumstances could arise if the proposed name includes a word that can only be spelled in the English language using a stem in the position designated by USAN. For example, if a proposed proprietary name includes the word "Congestion," the use of the letters "gest", which are also a USAN stem, is unavoidable.

F. Same Proprietary Name for Products Containing Different Active Ingredients

Sponsors should not use the same proprietary name or the same **root proprietary name** for products that do not contain at least one common active ingredient contained in the original

[14] The Joint Commission's Official "Do Not Use" List of Abbreviations, 2001, available at http://www.jointcommission.org/assets/1/18/Official_Do_Not_Use_List_6_111.PDF.

[15] The Institute for Safe Medication Practices' List of Error-Prone Abbreviations, Symbols, and Dose Designations, 2010, available at http://www.ismp.org/tools/errorproneabbreviations.pdf.

[16] See the list of approved USAN stems, available at http://www.ama-assn.org/ama/pub/physician-resources/medical-science/united-states-adopted-names-council/naming-guidelines/approved-stems.page.

marketed product. When two or more products have the same name and do not share any active ingredients in common with the original marketed product, end users may be confused about the products' ingredients and how each product should be used. In some cases, the name has led to the use of products at the wrong dose, for the wrong indication, in the wrong patient population, or in a contraindicated manner. Such name confusion errors have resulted in serious adverse reactions when patients were medicated in error with an active ingredient that was not intended to be administered.

G. Reuse of Proprietary Names

Sponsors should not reuse the proprietary name of a discontinued product when marketing a different drug or biological product because there is a strong risk that users may continue to associate the name with the original discontinued product. Proprietary names are used in prescribing for an extended period of time after product discontinuation.[17] Proprietary names associated with discontinued drug products also may continue to appear in drug product reference texts for extended periods of time.

IV. OTHER NAMING ATTRIBUTES THAT MIGHT BE CONSIDERED MISLEADING OR ERROR PRONE

In addition to the preliminary screening recommendations described in section III, sponsors should consider other important attributes during development of a proposed proprietary name before proceeding with a full assessment of safety and misbranding concerns and, when applicable, submission to FDA for review. FDA will closely scrutinize each proposed proprietary name for these attributes on a case-by-case basis, and the Agency can reject a name that is determined to be misleading or prone to medication errors.

A. Names That Include Reference to Product-Specific Attributes

FDA recommends that sponsors avoid incorporating product-specific attributes, such as manufacturing characteristics (e.g. "NameLyophylized"), dosage form (e.g. "Nametabs") or route of administration (e.g. "Nameoral"), as part of the proposed proprietary name. Including references to product-specific attributes in the root proprietary name may be acceptable if the product-specific attribute is consistent with the terminology used in the product's labeling and does not pose additional risks for medication error. However, in developing the names that include or make reference to product-specific attributes, companies may wish to consider that future changes in dosage form or route of administration or manufacturing characteristics may render the original proprietary name inaccurate. For flexibility in product development, it may be advisable to limit the inclusion of such attributes in the proposed proprietary name.

[17] Tu, CM, Taylor, K, and Chai, G. 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.

B. Dosing Interval

We generally discourage sponsors from adopting proprietary names that refer to product dosing interval, such as "NameQD" or "NameBID," even when the name accurately reflects the product's dosing instructions. This information is subject to change during the course of application review and during marketing if the approval of new dosing intervals, formulations, indications, or use in different patient populations (such as individuals with renal impairment) causes the original proprietary name to then be misleading.

It might be appropriate for a proprietary name to incorporate a reference to the product's dosing interval in conjunction with the root proprietary name (see section IV.D), such as "Name 24 hour." For example, if a sponsor markets several over-the-counter (OTC) drug products with different dosing intervals, proprietary names that include this information (such as "Name 12 hour" and "Name 24 hour") might help consumers distinguish between the products and appropriately select and administer the correct drug. However, these exceptions are handled on a case-by-case basis and might require FDA to review clinical or chemistry data submitted to support the drug approval in making its decision.

C. Modifiers as Components of a Proprietary Name

Some proprietary names are constructed of a root proprietary name modified by added words or components, which are referred to as **modifiers**. The modifier portion of a proprietary name might consist of one or more letters, numbers, and/or words, and might be attached to the beginning, middle, or end of the proprietary name. Sponsors frequently name multiple products containing at least one common active ingredient within a product line by using a common root proprietary name with various modifiers to distinguish products from one another.

Most often modifiers are used to convey distinguishing product characteristics, such as "Name ODT," for orally disintegrating tablets, or "Name XR," to signal that the product is an extended-release formulation. However, inconsistent use of modifiers and the absence of a standardized meaning for such terms can be confusing to end users. Misinterpretation of the intended meaning of the modifier has led to medication errors, such as dispensing and administering the wrong drug, wrong formulation, wrong dose, wrong strength, or wrong frequency of administration. 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.

To reduce the risk of medication errors associated with nonstandardized modifiers in proprietary names, FDA strongly encourages sponsors to, whenever possible, use an existing modifier with an established meaning that has not been a source of confusion.

The following considerations are intended to help sponsors with this assessment:

1. What should sponsors consider in the selection and evaluation of a modifier?

Sponsors should consider the following points carefully when deciding whether or not to include a modifier in a proprietary name and when evaluating the potential risk of a medication error associated with a specific proposed modifier.

- Do you currently market one or more products under the proposed root proprietary name? If so, evaluate the similarities and differences between the proposed product and the existing product(s). You should consider how to minimize the risk of confusion among the products, especially if the products have overlapping characteristics (such as immediate-release and extended-release products with the same active ingredient and dosage strength). You should also consider the potential for product confusion if the modifier is omitted by the prescriber or overlooked during dispensing or administration.

- If a proposed modifier describes a product characteristic, does it accurately describe the pertinent characteristic of your product?

- What is the rationale for the proposed modifier? Is it intended to differentiate the proposed product from other products or to convey a characteristic of the proposed product? Would marketing the proposed product without a modifier or under a different proprietary name raise concerns that could be addressed by an effective modifier in the proprietary name? In some cases, it may be preferable to use a modifier affixed to an existing name.

- Where will the modifier be placed in relation to the root proprietary name? What is the rationale for this placement?

- What is the modifier's intended meaning? Are there data to support that healthcare professionals and consumers understand this meaning?

- Is the proposed modifier currently used in the marketplace? We recommend checking the ISMP's most current List of Products with Drug Name Suffixes and other drug information references to determine whether the proposed modifier already is used in the marketplace and whether it has been used consistently with a commonly recognized meaning.[18] If an existing modifier with the same intended meaning is in the marketplace and familiar to and understood by end users without error, it might be appropriate to adopt the existing modifier. When deciding whether to use a different modifier instead of an existing modifier with the same intended meaning, you should consider whether the proposed modifier conveys the intended meaning as clearly as, or more clearly than, the existing modifier.

- Is there a risk that end users could misinterpret the modifier's intended meaning? What is the risk of medication errors if an end user confuses the modifier with some other

[18] See ISMP's List of Products With Drug Name Suffixes, 2010, available at http://www.ismp.org/Tools/drugnamesuffixes.pdf.

element of a prescription or order (such as frequency, strength, route of administration)? What is the risk if the modifier is omitted?

2. What specific issues should sponsors consider with modifiers?

a. Use of Numerals as Modifiers

FDA generally discourages the use of numerals within a proprietary name. Both Roman and Arabic numerals have been mistaken for the strength, quantity, duration, or controlled substance class of prescription drug products. For example, using the number "3" in a proprietary name, to represent the product strength, might be misinterpreted to mean that *three* tablets are administered or that the product should be used for only *three* days when the name appears in a drug order or prescription.

b. Device-Related Modifiers

Some proprietary name modifiers associated with new drug application (NDA), biologics license application (BLA), or abbreviated new drug application (ANDA) products represent the delivery device component of a combination drug-device or biological-device product. Such modifiers are reviewed as part of CDER's or CBER's proprietary name evaluation. For example, a product integrating a drug and a disposable injector device might use a root proprietary name for the drug component with the modifier "Pen" for the device component. Generally speaking, modifiers used to represent a device component can either be a general term for the type of device (sensical modifiers), such as "Pen," "Prefilled Syringe," or "Inhaler," or a sponsor-coined term (nonsensical modifiers), such as "SoloStar®" or "Diskus®." A sensical modifier might be suitable for use with a variety of products, as well as devices that operate differently from previously marketed devices. Similarly, a nonsensical modifier might be suitable for use with a variety of products, provided that the root proprietary name representing the drug name is adequately differentiated and the device platform operates the same across the various drug products. In either case, the device modifier must not render the combined proprietary name misleading by virtue of implying unique effectiveness or composition (21 CFR 201.10(c)(3)).

A final consideration for device modifiers relates to introducing a new device that delivers a drug, including a drug that is a biological product, that operates similarly, but not identically, to a previously marketed device. For example, if a sponsor is developing a drug-device combination product or a biological product-device combination product that includes a new disposable injector device that calls for a different set of tasks in order to perform an injection, it might be prudent to consider using a different modifier to represent the new combination product so that prescribers and patients are aware that the new combination product operates differently.

c. Descriptive Modifiers

Descriptive modifiers are words that describe some aspect of the product (e.g., indication, formulation, patient population) that are affixed to a root name of a product. Such modifiers are common with OTC products, but also may be used for prescription drug products. Concerns

sometimes arise with descriptive modifiers that are ambiguous, misleading, or subject to misinterpretation. A primary factor in evaluating the appropriateness of a modifier associated with a proprietary name is whether the modifier's intended meaning is supported by the proposed labeling and whether it is understood by the end user. For example, the labeling of a product as *Children's* may be considered misleading if the product is also intended to be used by infants and/or adults.

D. Brand Name Extensions

Proprietary names that include **brand name extensions** are evaluated on a case-by-case basis for both OTC and prescription products. Each request for review of a proposed proprietary brand name extension will be evaluated to consider whether the:

- products share at least one common active ingredient
- products are differentiated by labeling (carton and container)
- modifiers used are appropriate and effectively differentiate the product among members of the same product line

In some cases, brand name extensions have posed problems when the same root proprietary name is used for multiple products without modifiers that adequately differentiate among the products. Some brand name extensions have complicated the process of identifying and properly selecting an appropriate product by creating or reinforcing a false belief among consumers and healthcare professionals that all products with a shared root proprietary name also have the same active ingredients or same therapeutic indication for use.[19] The potential for confusion among products with the same root proprietary name might also be reinforced by visual cues created by the use of uniform trade dress and/or store displays that group products by brand name rather than by active ingredients or intended uses. The types of errors that have resulted from brand name extension confusion with products include the use of the product for the wrong indication, the administration of an unnecessary active ingredient, and the use of a product in the wrong patient population.

E. Dual Proprietary Names

Using distinct proprietary names for products that contain the identical active ingredient(s) but have different indications of use could pose potential safety risks. Safety concerns could arise, for example, if practitioners are unaware that two products prescribed for concomitant use contain the same active ingredient. This could lead to overdose or dose-related adverse reactions. Another risk may be if a drug-drug interaction is not noted because the healthcare professional and patient are unaware that a product sold under a proprietary name contains the same drug as another product with a different proprietary name. FDA will evaluate these proposals on a case-by-case basis along with any associated labeling that might address these potential risks.

[19] ISMP Medication Safety Alert! Acute Care Edition. 2004: Vol. 9 (issue 7): 1-2.

F. Proprietary Names of Drug Products Marketed Outside the United States

Medication errors resulting in dispensing and administration of the wrong drug have occurred when a proprietary name for a product marketed in the United States is identical, or virtually identical in spelling and pronunciation, to a foreign product containing an entirely different active ingredient marketed in a foreign country. For this reason, FDA recommends as a best practice against proposing a proprietary name that is identical or nearly identical to that of a marketed foreign product that contains an entirely different active ingredient, even if the proposed product will be marketed only in the United States.

G. Prescription-to-OTC Switch

When a drug product is "switched" from prescription to over-the-counter (OTC) status, the proposed proprietary name for the OTC product might or might not be the same as the original (prescription) proprietary name. Continued use of the original proprietary name might be appropriate when there is a full switch (i.e., all indications, dosing, and strengths previously limited to prescription use will now all be available OTC). However, when the product switch is only partial (i.e., prescription-only status still applies to some indications, dosages, or strengths), it might be appropriate to market the OTC product under a different or modified proprietary name. The same considerations discussed in section IV.D (above) also would apply to modifiers used to distinguish between the OTC and prescription products. Alternatively, the sponsor can propose a completely new proprietary name for the OTC product, whether the switch was full or partial. FDA will evaluate these proposals on a case-by-case basis to determine whether this practice could pose potential safety risks.

H. Use of Symbols

FDA discourages sponsors from using symbols (i.e., "+" or "&") to link components in proprietary names because symbols can be misinterpreted or confusing (e.g., "+" can be read as "4").[20] Therefore, FDA encourages using words rather than symbols.

I. Incorporation of the Sponsor's Name

Proprietary names should not incorporate the sponsor's name across multiple products (e.g., "ABCName1," "ABCName2," "ABCName3"). This practice can result in creating multiple similar proprietary names, which might increase the risk of confusion among the products. The practice can be problematic when products are stored alphabetically in distributor or pharmacy locations or when products are ordered from alphabetized lists.

[20]The Institute for Safe Medication Practices' List of Error-Prone Abbreviations, Symbols, and Dose Designations, 2010, http://www.ismp.org/tools/errorproneabbreviations.pdf.

V. MISBRANDING REVIEW AND METHODS FOR EVALUATING SAFETY OF PROPOSED PROPRIETARY NAMES FOR DRUGS

Beyond the initial screening considerations described in sections III and IV above, FDA evaluates proposed proprietary names for additional safety and misbranding concerns. For either category, we believe that no single test or standard is adequate to determine whether or not a proposed proprietary name is appropriate. Rather, the current approach to name evaluation uses a combination of different and complementary tests.

A. Misbranding Review (Other Than Medication Error Prevention)

Although this guidance focuses primarily on safety-related aspects of proprietary names, such as avoiding potential confusion with the proprietary names of other products, FDA also reviews and might object to a proposed name if it may misbrand the product for reasons not solely related to medication error prevention.

Among other things, the FD&C Act provides that a drug is misbranded if its labeling is false or misleading in any particular (21 U.S.C. 352(a)). A proprietary name, which appears in labeling, could result in such misbranding if it is false or misleading, such as by making misrepresentations with respect to safety or efficacy. For example, a fanciful proprietary name may misbrand a product by suggesting that it has some unique effectiveness or composition when it does not (21 CFR 201.10(c)(3)).

In determining whether a name is misleading, common morphological and semantic associations are considered along with *phonesthemes* (the sound of the name) and *phonosemantics* (meaning conveyed by the sound of the word) of the name.

For example, FDA likely would object to a proposed proprietary name that contained the **prefix** *best* or that sounds like *best* because it implies superiority over other currently available therapies. The word "best" is defined as "most advantageous, suitable, or desirable." Therefore, a proposed proprietary name containing or sounding like such a word implies superiority by suggesting that it has advantages when compared to other available therapies and is better than other available therapies. In the absence of appropriate scientific evidence to support claims that the product is superior to other competing products currently on the market to treat the condition, such a proposed name would be misleading.

B. Safety Review

FDA's safety review of proprietary names focuses on the avoidance of end user error. When evaluating the safety of a proposed proprietary name, FDA considers many potential sources for error, including phonetic, spelling, and orthographic similarities, as well as others identified elsewhere in this guidance.

Specific evaluation methods that FDA currently employs, as well as methods that FDA recommends sponsors employ before submitting a proposed proprietary name for FDA review,

are described below. The descriptions include methods for identifying existing proprietary names that could be confused with the sponsor's proposed name, as well as methods for assessing the potential likelihood and effects of name-related medication errors.

1. Conduct Name Simulation Studies

FDA performs simulation studies within the Agency to test the response of healthcare professionals to proposed names. The studies we carry out are limited in scope because they only involve FDA staff. As such, while we are confident that FDA simulation studies are predictive of errors in actual use,[21] they may not be sufficiently sensitive to identify the risks associated with any name tested in our studies. For these reasons, FDA believes more comprehensive simulation studies would be useful and that the following elements should be considered when sponsors are planning to conduct simulation studies.

a. General Description of Simulation Studies

Generally, name simulation studies 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 valuable the results of the simulation testing. Name simulation tests should reflect the full range and variety of tasks involved in the prescribing, transcribing, dispensing, and administration of drugs, as well as tasks involved in consumer selection of OTC drugs. Simulations should include common and easily simulated characteristics of real use, such as using ruled or unruled paper, prescription pads, computer order entry, and telephone orders to approximate written, oral, and electronic prescribing in the setting of care for the proposed product (e.g., inpatient and outpatient settings, long-term care). Simulations also should approximate the diversity of real-world prescribing conditions by varying factors such as background noise, handwriting samples, different ink colors, directions for use, and different voices/accents. In addition, the simulation study should present the proprietary name with the corresponding product characteristics (e.g., strength, route, dosage, and frequency) that are likely to be used to communicate prescriptions and orders for the proposed product.

b. Study Design

A simulation study designed to detect close to a zero percent error rate with statistical significance would call for an extremely large sample size (e.g., a sample of ~26,000 to detect an error rate of 0.001 at the 0.05 significance level).[22] FDA recognizes that a study of this magnitude is not realistic. However, a well-designed parallel group observational study

[21] FDA believes our simulation studies have good predictive value when an error does occur because the likelihood of observing an error in such a small study is low, and therefore an occurrence within the study is likely to predict errors in actual use.

[22] This calculation was made to determine whether the error rate differs from 0.001 at a 0.05 significance level and 80 percent power, assuming the medication error rate of the sample is 0.0005.

consisting of the number of participants described below can provide useful insight into how a proposed proprietary name might perform in real world conditions. In such a study, each group represents different prescribing scenarios based on all of the potential prescribing conditions for the proposed product. For example, a scenario simulating a written order in an inpatient setting could include an order written by a physician using lined paper, then transcribed and entered into a computer by a unit clerk, then read and dispensed by a pharmacist, then read and administered by a nurse.

When performing simulation testing, both quantitative and qualitative data should be collected. Both types of data can be collected anywhere in the medication use system. For example, quantitative data might document how many times a participant interpreted a prescription correctly and how many times it was misinterpreted. Qualitative data should include any concerns or problems the participants thought of or encountered while going through the process (for example, no error occurred but a participant felt that an error could have occurred in the situation).

c. Participants

All participants in name simulation studies should be actively practicing healthcare professionals, such as prescribers, transcribers, pharmacists, or nurses who administer the products in the proposed use conditions for the product. Care should be taken to ensure that participants are representative of the full range of persons involved in a given scenario. The study also should simulate the full range of settings where the product could be used, such as community pharmacy, ambulatory care, hospital, or long-term care. For example, if the product will be dispensed in an inpatient setting, the participants should include, but not be limited to, inpatient pharmacists, pharmacy technicians, ward clerks and nurses. Even when evaluating proprietary names for specialty drugs, sponsors should consider including primary care practitioners, pharmacists, and nurses to probe which product names outside the specialty might cause error. These stakeholders will bring experience from different workflow and practice environments.

FDA generally does not consider it necessary to include patients in a name simulation study for a prescription product. However, consumers should be included in name simulation studies for OTC drugs.

d. Number of Scenarios

For an adequate descriptive assessment, sponsors should test a minimum of 20 scenarios, representing each possible prescribing condition for the proposed product (e.g., communication from physician to ward clerk to pharmacist to nurse). Participants involved in a name simulation study can participate in the testing of multiple proposed proprietary names. However, to minimize bias, a name should not be tested by the same participant more than once. The number of participants in each simulation scenario should reflect the actual number of participants in an actual clinical scenario. Generally, an individual test scenario will involve two to five participants (for example, physician-ward clerk - pharmacist - nurse).

Each anticipated prescribing condition for the proposed product should be tested several times, giving consideration to all relevant modes of communication (such as spoken, written, computer order entry, computer selection, and selection of product from drop down menu). For example, for a product that is administered only intravenously in an inpatient setting, an outpatient simulation using a handwritten prescription might not be helpful. A simulation for an orally administered product that could be dispensed in either inpatient or outpatient settings should contain all possible inpatient and outpatient scenarios. Table 1 shows example scenarios for an orally administered drug. For these example scenarios, we estimate that there should be approximately 70 participants because not all scenarios will involve the same number of participants (e.g., physician – pharmacist). Where appropriate, these scenarios should be revised to reflect, as closely as possible, the likely healthcare setting(s) for the use of the product, including how the product will be prescribed, how the prescription will be transcribed, and how the product will be dispensed and administered.

Sponsors should consider embedding the test name in a list of two or three other proprietary names of marketed products in the simulated prescriptions, or consider using other simulated prescription formats that are designed to mimic the results of real-world settings. Spoken orders should include several scenarios with an unaided pronunciation and several scenarios with a pronunciation based on how the applicant proposes to pronounce the name when marketed (for example, *Kaletra* is pronounced by some as Kuh-let-ra and the applicant's pronunciation is Kuh-lee-tra).

Table 1:
Example Scenarios for Name Simulation Study for an Orally Administered Drug

Scenario Number	Prescribing Condition	Participant Group
1	Inpatient: Written order on lined paper	physician A – ward clerk A – nurse A – pharmacist A – nurse B
2	Inpatient: Written order on lined paper	physician assistant A – ward clerk B – nurse C – pharmacist B – nurse D
3	Inpatient: Written order on lined paper	physician B – nurse E – pharmacist C – nurse F
4	Inpatient: Written order on lined paper	physician C – ward clerk C – nurse G – pharmacist D – nurse H
5	Inpatient: Spoken order transcribed to a written order unaided pronunciation	physician D – nurse I – ward clerk D – pharmacist E – nurse J
6	Inpatient: Spoken order transcribed to a written order unaided pronunciation	physician assistant B – nurse K – ward clerk E – pharmacist F – nurse L
7	Inpatient: Spoken order transcribed to a written order pronunciation as intended by applicant	physician E – nurse M – pharmacist G – nurse N
8	Inpatient: Spoken order transcribed to a written order pronunciation as intended by applicant	physician F – nurse O – ward clerk F – pharmacist H – nurse P
9	Inpatient: Direct computer entry	physician G – pharmacist I – nurse Q
10	Inpatient: Direct computer entry	physician assistant C – pharmacist J – nurse R
11	Inpatient: Direct computer entry	physician H – pharmacist K – nurse S

Table 1: Example Scenarios for Name Simulation Study for an Orally Administered Drug		
Scenario Number	**Prescribing Condition**	**Participant Group**
12	Inpatient: Direct computer entry	nurse practitioner A – pharmacist L – nurse P
13	Outpatient: Written prescription	nurse practitioner B – pharmacist M
14	Outpatient: Written prescription	physician I – pharmacist N
15	Outpatient: Written prescription	physician J – pharmacist O
16	Outpatient: Written prescription	physician assistant D – pharmacist P
17	Outpatient: Spoken prescription left on voice mail unaided pronunciation	nurse practitioner C – pharmacist Q
18	Outpatient: Spoken prescription left on voice mail unaided pronunciation	physician K – pharmacist R
19	Outpatient: Spoken prescription left on voice mail pronunciation as intended by applicant	nurse practitioner D – pharmacist S
20	Outpatient: Spoken prescription left on voice mail pronunciation as intended by applicant	nurse practitioner E – pharmacist T
21	Outpatient: Electronic generated prescription	physician L – pharmacist U
22	Outpatient: Electronic generated prescription	physician M – pharmacy technician A – pharmacist V
23	Outpatient: Electronic generated prescription	physician assistant E – pharmacist W
	Total Participants	70

At the end of a simulation, each participant should be interviewed using nonleading scripted follow-up questions. The participant responses should be recorded verbatim. All qualitative data derived from follow-up questioning should be coded and analyzed based on verbatim responses from the participants (see Table 2 for examples of verbatim responses grouped into categories). The verbatim responses might confirm or further describe a potential for confusion. More importantly, responses might identify additional names of concern that were not identified through a manual database or computational searches.

Table 2: Examples of Responses to Follow-up Questions		
Follow-up Questions	**Categorized Responses**	**Participants With Categorized Response**
Do you think this name looks like any other drug name? If yes which drug?	Yes No Brand X Brand Y	8 52 3 5
Do you think this name sounds like any other drug name? If yes, which drug?	Yes No Brand X	8 52 8
Do you think this name looks like any medical terms or laboratory tests? If yes, what terms or tests?	Yes No	0 60

Table 2: Examples of Responses to Follow-up Questions		
Follow-up Questions	**Categorized Responses**	**Participants With Categorized Response**
Do you think this name sounds like any medical terms or laboratory tests? If yes, what terms or tests?	Yes No	0 60
Describe your overall impression of the name. These comments do not necessarily have to be related to safety.	There are many drug names on the market that seem to start with ___. This name reminds me of _____. Good name; does not appear to be a problem. The name seems to conflict with what the drug is supposed to treat.	12 10 25 13

2. Obtain Medication Error Data

Case reports of medication errors help inform the analysis of a proposed proprietary name and overall product design (e.g., **packaging**, labels, and labeling). FDA searches databases containing medication error reports with the goal of identifying relevant information about problems and failures that lead to medication error, and the Agency applies any relevant information to the evaluation of a proposed proprietary name and product design prior to approval. FDA recommends that sponsors do the same. A sponsor can obtain medication error report information from its own safety databases and published literature.

In some cases, there is marketing experience with the proposed proprietary name outside of the United States. In these cases, if a sponsor obtains medication error information related to the product's established and proposed proprietary name that may be relevant to the use of the proposed proprietary names in the United States, this information should be provided to FDA in the proprietary name submission.[23]

3. Computational Method to Identify Names With Potential Orthographic, Spelling, and Phonetic Similarities

Once a proprietary name has been evaluated under the considerations outlined in sections III and IV of this guidance, FDA evaluates the proposed name against potentially similar names. In order to identify names with potential similarity to the proposed proprietary name, FDA enters the proposed proprietary name into the FDA's Phonetic and Orthographic Computer Analysis

[23] See 21 CFR 312.32(b). Current regulations require sponsors, when submitting an application, to submit a review of all information relevant to the safety of the product from any source, foreign or domestic, including information derived from clinical or epidemiological investigations, commercial marketing experience, reports in the scientific literature, unpublished scientific papers, and reports from foreign regulatory authorities.

(POCA) system and queries the name against drug reference databases (e.g., Drugs@FDA and RxNorm).

Additionally, FDA will compare the proposed proprietary name to other proposed proprietary names submitted to the agency for products not yet approved. Such names are often confidential; therefore, it is possible that FDA may identify conflicts with pending products of which the general public is not aware.[24]

FDA recommends that sponsors screen their proposed names in by conducting orthographic and phonetic searches using the POCA system developed by FDA. We recommend that you use POCA to search databases that encompass a large number of drug products such as Drugs@FDA and another database that captures a reasonable representation of OTC drugs (e.g., RxNorm).

If the proposed name contains a modifier, first enter the root proprietary name without the modifier and group the names as described below. Then repeat this process using the root name and modifier.

The POCA search will provide three data sets: COMBINED orthographic and phonetic matches, phonetic matches, and orthographic matches. Sponsors should then review the COMBINED orthographic and phonetic matches and group the name pairs into one of the following three categories:

- Highly Similar Pair: combined match percentage score ≥70%.
- Moderately Similar Pair: combined match percentage score ≥50% to ≤ 69%.
- Low Similarity: combined match percentage score ≤49%.

4. Safety Determination of Names With Potential Orthographic, Spelling, and Phonetic Similarities

The acceptability of the proposed proprietary name from a look-alike and sound-alike perspective is reviewed using the criteria outlined in checklists in Appendices D, E, and F, which correspond to each of the three categories (Highly Similar Pair, Moderately Similar Pair, and Low Similarity) described in section V.B.3. The intent of these checklists is to increase the transparency and predictability of the safety determination of whether a proposed name is vulnerable to confusion from a look-alike or sound-alike perspective. Each bullet below corresponds to the name similarity category determined in section V.B.3 and cross-references the

[24] Proposed names may be associated with drug products related to investigational new drug applications (INDs), NDAs, BLAs, or ANDAs. In those rare instances when a conflict is identified with a proposed proprietary name of a pending drug application, FDA will accept the proposed name of whichever product is approved first and notify the other applicant that they must seek a new name. The ultimate acceptability of a proposed proprietary name that conflicts with other proposed proprietary names is *dependent upon which underlying application is approved first*. If another product is approved prior to your product, with a name that would be confused with your proposed proprietary name, you will be requested to submit another name.

respective appendix that addresses criteria that FDA uses to determine whether a name presents a safety concern from a look-alike or sound-alike perspective.

- For highly similar names, differences in product characteristics often cannot mitigate the risk of a medication error, including product differences such as strength and dose. Thus, proposed proprietary names that have a combined score of ≥ 70 percent are at risk for a look-alike sound-alike confusion, which is an area of concern for FDA. (See Appendix D.)
- Moderately similar names with overlapping or similar strengths or doses represent an area for concern for FDA. The dose and strength information is often located in close proximity to the drug name itself on prescriptions and medication orders, and the informationcan be an important factor that either increases or decreases the potential for confusion between similarly named drug pairs. The ability of other product characteristics to mitigate confusion (e.g., route, frequency, dosage form) may be limited when the strength or dose overlaps. FDA will review such names further, to determine whether sufficient differences exist to prevent confusion. (See Appendix E.)
- Names with low similarity that have no overlap or similarity in strength and dose are generally acceptable (see Appendix F) unless there are data to suggest that the name might be vulnerable to confusion (e.g., prescription simulation study suggests that the name is likely to be misinterpreted as a marketed product). In these instances, we would reassign a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist. (See Appendix E.)

5. Final Determination of the Acceptability of a Proposed Proprietary Name

The final determination on the acceptability of a proposed proprietary name is based on FDA's review of all information and analyses described in this guidance, along with any information submitted by the sponsor. 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. Appendix B provides a flow chart that summarizes the considerations for developing and selecting a proposed proprietary name.

C. Name Review for Nonprescription Drug Products

Nonprescription (OTC) drug products are routinely selected, purchased, and used by consumers without the involvement of a healthcare professional. These products often are recommended to consumers by healthcare professionals using a proprietary name. For these reasons, it is critical to ensure that the proprietary name is not subject to confusion by either healthcare professionals or consumers.

FDA reviews proposed proprietary names for OTC drugs that will be marketed under an NDA or ANDA as part of the NDA or ANDA approval process. However, many OTC drugs are not

reviewed and approved by FDA prior to marketing, but are marketed instead under an applicable OTC drug monograph and related general regulations for OTC drugs.[25] Regardless of which regulatory framework governs market entry of a particular OTC drug, as a best practice we recommend that proprietary names of OTC drugs be evaluated by the manufacturers for safety using the methods described in section V.B before marketing, taking into account other considerations discussed below.

1. Multiple Products With a Shared "Family Name"

Many OTC drugs are marketed as part of a line or family of products containing one of the active ingredients present in the first marketed product. The products often share the same root proprietary name with a **suffix** or other modifier to distinguish individual products. Because this practice creates inherent similarity among the names, these products may be subject to name confusion and medical error. Section IV.E outlines the safety concerns FDA has with brand name extensions, and these considerations also apply to OTC products. Thus, it is essential that consumers are able to identify an appropriate product at the point of purchase based on the product name and other information on the **principal display panel** as defined in 21 CFR 201.60.

2. Other Name Testing Considerations for OTC Drugs

Proprietary names for OTC drugs should be evaluated using simulation studies designed to test both consumer and healthcare professional understanding of the proposed name. It may be important to evaluate whether participants can interpret both written and oral communication of the name to select the intended product. Differing study designs might be appropriate, depending on proposed product characteristics, patient population, or other product-specific considerations, and it may not be possible to design a single study that can address all possible scenarios. Thus, for proprietary names submitted as part of an application, FDA is willing to meet with sponsors to discuss different protocols that can be used to test a proposed proprietary name for a specific product(s) prior to submission.

FDA recommends applying the following general principles when testing an OTC drug proprietary name in consumer and healthcare professional populations:

- Always include consumers in simulation testing of OTC drug names.
- Assess whether or not a proposed proprietary name overstates the safety or effectiveness of the product or is otherwise confusing or misleading. Aspects to consider include, but

[25] An OTC drug monograph is an FDA regulation that identifies active ingredients, labeling, and other required conditions for all products within a given therapeutic class, such as cough-cold or sunscreen products. To be marketed without an approved NDA, an OTC drug product must comply with an applicable final monograph and general regulations for OTC drugs, as described in 21 CFR 330.10. Additional information about the OTC drug monograph system and other aspects of OTC drug regulation can be found on FDA's Web site at http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ucm209647.htm.

are not limited to, whether or not a proprietary name implies an indication or use, active ingredient, dosing frequency, population, route of administration, or duration of effect that is inconsistent with the proposed labeling.

- Incorporate nonleading and filter questions into the evaluation questionnaires (e.g., "Does the name tell you what the product is used for? Yes or No." If yes, "What does it tell you it is used for?").

- Note that all OTC proposed proprietary drug product names submitted under a NDA or ANDA are assessed for potential consumer safety issues related to the entire package label prior to approval.[26]

- When a proprietary name is the name of a family of products, with multiple product names differing only by the suffix, it is even more important that the information on the principal display panel enable the consumer to differentiate products at the point of purchase.

- In addition to the proprietary name, the presentation of information on the package might be inadequate, leading to consumer confusion and potential medication errors. Concerns include, but are not limited to, the following: information might be presented in a confusing manner, the package might lack important information for proper use, or the principal display panel might not present the information so that a consumer can differentiate the product from other similar products and use it correctly. Consult the labeling regulations (21 CFR 201.60, 201.61 and 201.62) for the type of information that is required on the principal display panel of an OTC drug product. This information is important in ensuring that the consumer is not misled and can accurately self-select and use the product.

[26] See FDA guidance for industry *Label Comprehension Studies for Nonprescription Drug Products.*

GLOSSARY

Assimilation or deletion: Assimilation is a change of a sound in speech so that it becomes identical with or similar to a neighboring sound. An example of assimilation is when the \z\ assimilates to \sh\ in the phrase *his shoe*. Deletion occurs when a sound is omitted in pronunciation. Deletion usually occurs within the initial syllable of a word following at least one consonant and followed by a stressed syllable. Examples of deletion would include *garage to – grage* and *surround* to – *sround*. Deletion and assimilation can occur together, and often do, as the assimilation of one feature of a neighboring sound will make that sound less phonologically necessary and make its deletion more probable.

Brand name extension: *Brand name extension* is a term used to describe the reuse of an already-marketed proprietary name with the addition of a modifier to introduce a new product. Brand name extensions might also be referred to as *Family Trade Names* or *Umbrella Names*.

Container closure system: A *container closure system* refers to the sum of packaging components that together contain and protect the dosage form. This includes primary packaging components and secondary packaging components, if the latter are intended to provide added protection to the drug product. A packaging system is equivalent to a container closure system.

End user: The term *end user* includes, but is not limited to, the patient, patient's caregiver, the prescribing physician, nurse, pharmacist, pharmacy technician, and other individuals who are involved in routine procurement, stocking, storage, and administration of medications (e.g., medication technicians).

Established name: Section 502(e)(3) of the FD&C Act (21 U.S.C. 352(e)(3)) states that:

> the term "established name," with respect to a drug or ingredient thereof, means (A) the applicable official name designated pursuant to section 508, or (B) if there is no such name and such drug, or such ingredient, is an article recognized in an **official compendium**, then the official title thereof in such compendium, or (C) if neither clause (A) or clause (B) of this subparagraph applies, then the common or usual name, if any of such drug or such ingredient, except that where clause (B) of this subparagraph applies to an article recognized in the United States Pharmacopeia and in the Homeopathic Pharmacopoeia under different official titles, the official title used in the United States Pharmacopeia shall apply unless it is labeled and offered for sale as a homeopathic drug, in which case the official title used in the Homeopathic Pharmacopoeia shall apply(emphasis added)

Infix: An *infix* is a group of letters that appears in the middle of the proprietary name.

Label: As defined in section 201(k) of the FD&C Act (21 U.S.C. 321(k)), the term *label* means "a display of written, printed, or graphic matter upon the immediate container of any article." If any word, statement, or other information is required by the FD&C Act to appear on the label, it must appear on the outside container or wrapper, if there is one, or be "easily legible through the outside container or wrapper."

Labeling: As defined in section 201(m) of the FD&C Act, the term *labeling* means "all labels and other written, printed, or graphic matter (1) upon any article or any of its containers or wrappers, or (2) accompanying such article."

Modifier: A *modifier* is a portion of the proprietary name. Some proprietary names are constructed of a root name and added word(s) or other components that are referred to as the modifier portion of the proprietary name. The modifier portion of a proprietary drug name might be a letter, number, word, device name, or combination of letters, numbers, and words attached to the beginning, middle, or end of a root proprietary drug name.

Official compendium: The term *official compendium* is defined in section 201(j) of the FD&C Act as "the official United States Pharmacopoeia, official Homeopathic Pharmacopoeia of the United States, official National Formulary, or any supplement to any of them."

Packaging: A *package* or *market package* refers to the container closure system and labeling, associated components (e.g., dosing cups, droppers, spoons), and external packaging (e.g., cartons or shrink wrap). A market package is the article provided to a pharmacist or retail customer upon purchase and does not include packaging used solely for the purpose of shipping such articles.

Prefix: A *prefix* is a group of letters that appears in the beginning of the proprietary name.

Principle display panel: As defined by 21 CFR 201.60, the term *principal display panel,* as it applies to over-the-counter drugs in package form and as used in this part, means the part of a label that is most likely to be displayed, presented, shown, or examined under customary conditions of display for retail sale.

Proper name: For biological products, the term *proper name* means the name designated in the license for use upon each package of the product (21 CFR 600.3(k)).

Proprietary name: The *proprietary name* is the exclusive name of a drug product owned by a company under trademark law regardless of registration status with the U.S. Patent and Trademark Office.

Root proprietary name: The term *root proprietary name* refers to the portion of a proposed proprietary name, generally within a product line extension, that is or has already been marketed.

Suffix: A *suffix* is a group of letters that appears at the end of the proprietary name.

Vowel reduction: Vowel reduction is any of various changes in the acoustic quality of vowels, which are related to changes in stress, sonority, duration, loudness, articulation, or position in the word, and which are perceived as "weakening." It most often makes the vowels shorter as well.

Appendix A: Databases and Other Resources

In most cases, the computerized resources listed here are publicly available.

FDA Adverse Event Reporting System (FAERS)

The FDA Adverse Event Reporting System (FAERS) is a database that contains information on adverse event and medication error reports submitted to FDA. The database is designed to support the FDA's postmarket safety surveillance program for drug and therapeutic biological products. The informatic structure of the FAERS database adheres to the international safety reporting guidance issued by the International Conference on Harmonisation. Adverse events and medication errors are coded to terms in the Medical Dictionary for Regulatory Activities (MedDRA) terminology. Product names are coded using the FAERS Product Dictionary. More information about FAERS can be found at: http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/default.htm.

Vaccine Adverse Event Reporting System (VAERS)

VAERS is a postmarket vaccine safety surveillance program cosponsored by the Centers for Disease Control and Prevention (CDC) and FDA. VAERS collects information about adverse events that occur after the administration of U.S. licensed vaccines. The VAERS Web site provides a nationwide mechanism by which adverse events following immunization can be reported, analyzed, and made available to the public. The VAERS Web site also provides a vehicle for disseminating vaccine safety-related information to parents or guardians, healthcare professionals, vaccine manufacturers, state vaccine programs, and other constituencies. The majority of VAERS reports are received from vaccine manufacturers and healthcare professionals.

Phonetic and Orthographic Computer Analysis (POCA)

POCA is a system designed by FDA. As part of the name similarity assessment, POCA is used to evaluate proposed names via a phonetic and orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. Likewise, an orthographic algorithm exists that operates in a similar fashion. POCA is publicly available by requesting the system from FDA .

Drugs@FDA

Drugs@FDA, available at [http://www.fda.gov/Drugs/InformationOnDrugs/ucm135821.htm], is an FDA Web site that contains most of the drug products approved in the United States since 1939. The majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present. Drugs@FDA contains official information about FDA-approved *brand name* and *generic drugs*; *therapeutic biological products*, *prescription* and *over-the-counter* human drugs; and *discontinued drugs* (see Drugs @ FDA Glossary of Terms, available at http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm#ther_biological).

Center for Biologics Evaluation and Research (CBER) Products

The CBER products Web site is publically available and contains most of the biological products currently regulated by CBER. Many of the labels, approval letters, reviews, and other information are available for products approved from 1996 to the present (http://www.fda.gov/cber/products.htm).

Electronic online version of FDA's Orange Book

This Orange Book Web site is publically available and provides a compilation of approved drug products with therapeutic equivalence evaluations (http://www.fda.gov/cder/ob/default.htm).

RxNorm

RxNorm is publically available and contains the names of prescription and many OTC drugs available in the United States. RxNorm includes generic and branded drug products and packaging configurations. Radiopharmaceuticals, contrast media, food, dietary supplements, and medical devices, such as bandages and crutches, are all out of scope for RxNorm (http://www.nlm.nih.gov/research/umls/rxnorm/overview.html#).

United States Patent and Trademark Office (USPTO)

The USPTO's Web site is publically available and provides information regarding marketed and pending patents and trademarks (http://www.uspto.gov).

USAN Stems

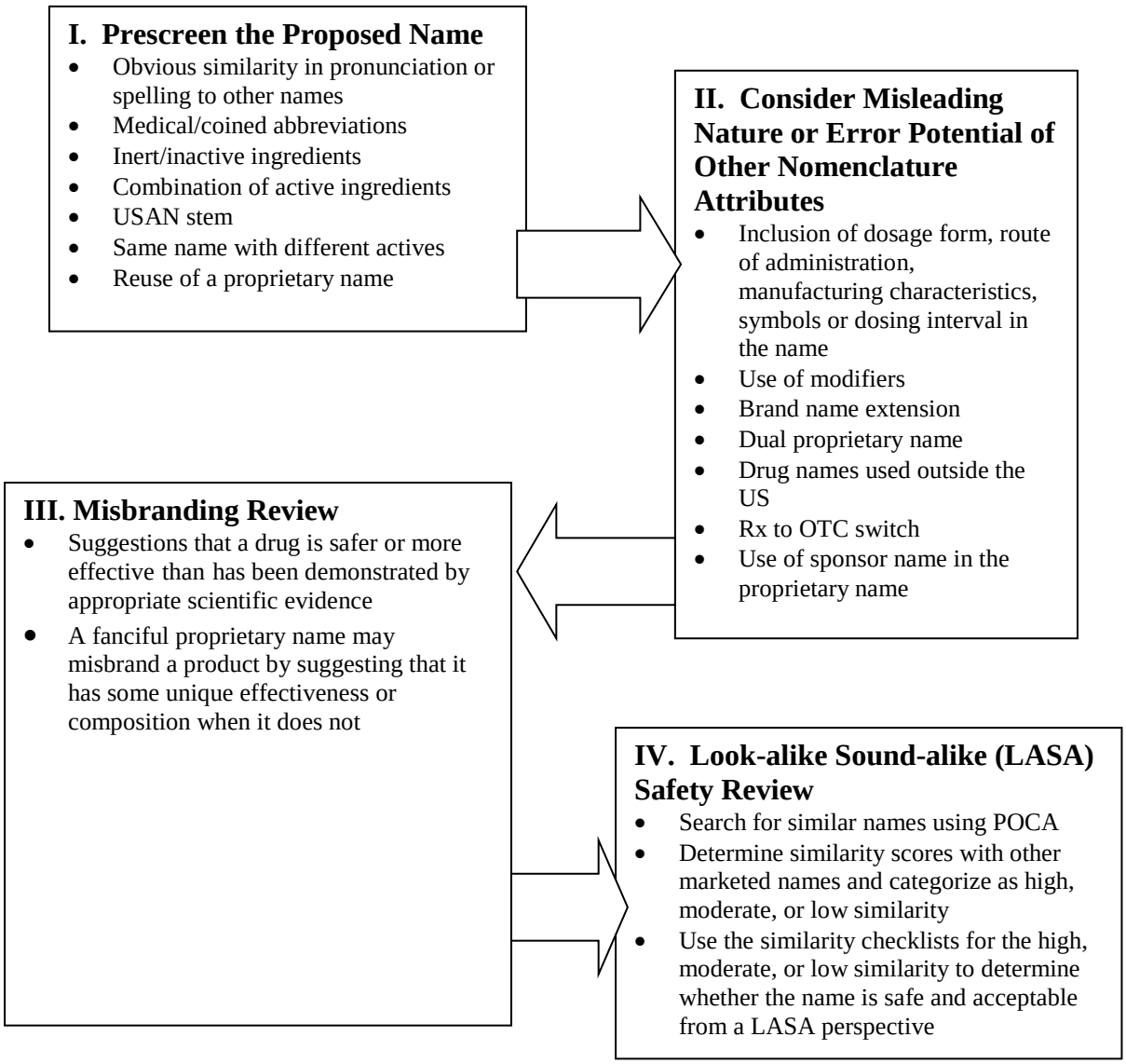
The USAN Council (tri-sponsored by the American Medical Association (AMA), the United States Pharmacopeial Convention, and the American Pharmacists Association) aims for global standardization and unification of drug nomenclature and related rules to ensure that drug information is communicated accurately and unambiguously, working closely with the International Nonproprietary Name Programme of the World Health Organization, and various national nomenclature groups. This Web site is publically available, managed by the

AMA, and contains lists of all of the recognized USAN stems (http://www.ama-assn.org/ama/pub/category/4782.html).

Medical Abbreviations References

Various references on this topic are available for purchase from private sources. These references contain commonly used medical abbreviations and their definitions.

Appendix B: Overview of Considerations for Evaluating a Proposed Proprietary Name



Appendix C: Prescreening Checklist for Proposed Proprietary Name

	Answer the questions in the checklist below. Affirmative answers to any of these questions indicate a potential area of concern that should be carefully evaluated as described in this guidance.
Y/N	**Is the proposed name obviously similar in spelling and pronunciation to other names?**
	Proprietary names should not be similar in spelling or pronunciation to proprietary names, established names, or ingredients of other products.
Y/N	**Are there medical and/or coined abbreviations in the proprietary name?**
	Proprietary names should not incorporate medical abbreviations (e.g., QD, BID, or others commonly used for prescription communication) or coined abbreviations that have no established meaning.
Y/N	**Are there inert or inactive ingredients referenced in the proprietary name?**
	Proprietary names should not incorporate any reference to an inert or inactive ingredient in a way that might create an impression that the ingredient's value is greater than its true functional role in the formulation (21 CFR 201.10(c)(4)).
Y/N	**Does the proprietary name include 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)).
Y/N	**Is there a United States Adopted Name (USAN) stem in the proprietary name?**
	Proprietary names should not incorporate a USAN stem in the position that USAN designates for the stem.
Y/N	**Is this proprietary name used for another product that does not share at least one common active ingredient?**
	Drug products that do not contain at least one common active ingredient should not use the same (root) proprietary name.
Y/N	**Is this a proprietary name of a discontinued product?**
	Proprietary names should not use the proprietary name of a discontinued product if that discontinued drug product does not contain the same active ingredients.

Appendix D: Highly Similar Name Pair Checklist

Highly Similar Name Pair Checklist (i.e., COMBINED Orthographic/Phonetic score is ≥ 70%).

Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may render the names less likely to confusion, provided that the pair do not share a common strength or dose.			
Orthographic Checklist		Phonetic Checklist	
Y/N	Do the names begin with different first letters? *Note that even when names begin with different first letters, certain letters may be confused with each other when scripted.*	**Y/N**	Do the names have different number of syllables?
Y/N	Are the lengths of the names dissimilar* when scripted? **FDA considers the length of names different if the names differ by two or more letters.*	**Y/N**	Do the names have different syllabic stresses?

Y/N	Considering variations in scripting of some letters (such as *z* and *f*), is there a different number or placement of upstroke/downstroke letters present in the names?	**Y/N**	Do the syllables have different phonologic processes, such as **vowel reduction**, **assimilation**, or **deletion**?
Y/N	Is there different number or placement of cross-stroke or dotted letters present in the names?	**Y/N**	Across a range of dialects, are the names consistently pronounced differently?
Y/N	Do the **infixes** of the name appear dissimilar when scripted?		
Y/N	Do the suffixes of the names appear dissimilar when scripted?		

930
931

Appendix E: Moderately Similar Name Pair Checklist

Moderately Similar Name Pair Checklist (i.e., combined score is ≥50% to ≤69%).

Step 1	Review the DOSAGE AND ADMINISTRATION and HOW SUPPLIED/STORAGE AND HANDLING sections of the prescribing information (or for OTC drugs refer to the Drug Facts label) to determine if strengths and doses of the name pair overlap or are very similar. Different strengths and doses for products whose names are moderately similar may decrease the risk of confusion between the moderately similar name pairs. Name pairs that have overlapping or similar strengths or doses have a higher potential for confusion and should be evaluated further (see Step 2). Because the strength or dose could be used to express an order or prescription for a particular drug product, overlap in one or both of these components would be reason for further evaluation. For single strength products, also consider circumstances where the strength may not be expressed. For any drug products comprised of more than one active ingredient, consider whether the strength or dose may be expressed using only one of the components. To determine whether the strengths or doses are similar to your proposed product, consider the following list of factors that may increase confusion: o Alternative expressions of dose: 5 mL may be listed in the prescribing information, but the dose may be expressed in metric weight (e.g., 500 mg) or in non-metric units (e.g., 1 tsp, 1 tablet/capsule). Similarly, a strength or dose of 1000 mg may be expressed, in practice, as 1 g, or vice versa. o Trailing or deleting zeros: 10 mg is similar in appearance to 100 mg which may potentiate confusion between a name pair with moderate similarity. o Similar sounding doses: 15 mg is similar in sound to 50 mg
Step 2	Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may reduce the likelihood of confusion for moderately similar names **with** overlapping or similar strengths or doses.

	Orthographic Checklist (Y/N to each question) • Do the names begin with different first letters? Note that even when names begin with different first letters, certain letters may be confused with each other when scripted. • Are the lengths of the names dissimilar* when scripted? *FDA considers the length of names different if the names differ by two or more letters. • Considering variations in scripting of some letters (such as *z* and *f*), is there a different number or placement of upstroke/downstroke letters present in the names? • Is there different number or placement of cross-stroke or dotted letters present in the names? • Do the infixes of the name appear dissimilar when scripted? • Do the suffixes of the names appear dissimilar when scripted?	Phonetic Checklist (Y/N to each question) • Do the names have different number of syllables? • Do the names have different syllabic stresses? • Do the syllables have different phonologic processes, such as vowel reduction, assimilation, or deletion? • Across a range of dialects, are the names consistently pronounced differently?

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936
937

Appendix F: Low Similarity Name Pairs

Low Similarity Name Pairs (i.e., combined score is ≤49%).

In most circumstances, these names are viewed as sufficiently different to minimize confusion. Exceptions to this would occur in circumstances where, for example, there are data that suggest a name with low similarity is nonetheless misinterpreted as a marketed product name in a prescription simulation study. In such instances, FDA would reassign a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.