

**Best Practices in Developing
Proprietary Names for Human
Prescription Drug Products**

Guidance for Industry

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

**December 2020
Drug Safety**

Best Practices in Developing Proprietary Names for Human Prescription Drug Products Guidance for Industry

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Guidance for Industry¹

Best Practices in Developing Proprietary Names for Human Prescription Drug Products

This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA office responsible for this guidance as listed on the title page.

I. INTRODUCTION

FDA is issuing this guidance to help sponsors of human prescription drug products² develop **proprietary names**³ for those products. This guidance describes best practices to help minimize proprietary name-related **medication errors** and otherwise avoid adoption of proprietary names that contribute to violations of the Federal Food, Drug, and Cosmetic Act (FD&C Act) and its implementing regulations. It also describes the framework FDA uses in evaluating proposed proprietary names that is also available to sponsors to use before submitting names for FDA review if they wish. This guidance does not address the designation of **established names** or **proper names**.

This guidance applies to all human prescription drug 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*.

FDA is separately developing guidance on best practices in developing proprietary names for nonprescription drug products.⁴

¹ This guidance was prepared by the Office of Surveillance and Epidemiology, Division of Medication Error Prevention and Analysis, and the Office of Prescription 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 For purposes of this guidance, unless otherwise specified, references to “drugs” and “drug products” include drugs submitted for approval or approved under section 505 of the FD&C Act (21 U.S.C. 355) and biological products licensed under section 351 of the Public Health Service Act (42 U.S.C. 262), other than devices regulated under a biologics license application.

³ Terms that appear in bold type upon first use are described in the Glossary, as they are used in this guidance.

⁴ See the FDA draft guidance for Industry *Best Practices in Developing Proprietary Names for Human Nonprescription Drug Products* (December 2020) for design practices to help minimize errors with nonprescription proprietary names. We update guidances periodically. For the most recent version of a guidance, check the FDA Drugs guidance web page, available at

<https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

When final, this guidance will represent the Agency’s current thinking on this topic.

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This guidance is intended to provide clarity and transparency to sponsors on the factors and systematic framework FDA uses to evaluate proposed proprietary names for prescription drugs and to recommend best practices for sponsors considering such names. Using the best practice recommendations and other assessment tools addressed in this guidance is not mandatory, and applying them does not dictate specific outcomes. Assessments of a proprietary name are necessarily fact-specific, and therefore, FDA's determinations are made on a case-by-case basis, considering the totality of the information.

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency'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 Agency's guidance means that something is suggested or recommended, but not required.

II. BACKGROUND

Selecting a proprietary name is a critical element in drug product design and development because **end users** may rely, in part or in whole, on the proprietary name to identify which product, among thousands of available products, is intended for or used by a particular patient. Proprietary names of drug products are commonly used by physicians and other health care professionals to prescribe or discuss a drug, and for this reason, accurate identification by the end user is essential. If end users cannot easily distinguish a proprietary name from other drug names that are similar phonetically (sound-alike names) or in their spelling or orthographic appearance (look-alike names), or if the drug name is 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.⁵ The report recommended that FDA encourage pharmaceutical companies to test proposed proprietary names to identify and remedy potential sound-alike and look-alike confusion with existing drug names.⁶ In July 2006, the IOM published a follow-up report titled *Preventing Medication Errors*, 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.^{7,8}

⁵ IOM, 1999, *To Err Is Human: Building a Safer Health System*. Institute of Medicine, National Academies Press: Washington, DC, 2000

⁶ IOM, 1999, *To Err Is Human: Building a Safer Health System*. 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).

^{7,8} IOM, 2006, *Preventing Medication Errors*, Institute of Medicine, National Academies Press: Washington, DC, 2006, Chapter 6, Recommendation 4, p. 274. pp. 281-282.

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As FDA has long recognized, and addressed on numerous occasions in recent decades, confusion involving proprietary names can cause or contribute to significant medication errors.⁹ Our focus has been to develop and communicate to sponsors a systematic, standardized, and transparent approach to proprietary name evaluation within the product development, 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) and in 2012 implemented BsUFA performance goals^{10,11} In 2008, the Agency held another public meeting to further discuss testing and evaluating proprietary names.

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.

Proprietary names are used in a product's **label** and **labeling**¹², including promotional labeling. A drug's labeling, in turn, is often a key element in FDA oversight. For example, under section 502(a) of the FD&C Act (21 U.S.C. 352(a)), a drug is misbranded if its labeling is false or misleading in any particular. Section 201(n) of the FD&C Act (21 U.S.C. 321(n)) sets forth certain considerations that shall be taken into account when determining whether labeling is misleading. FDA regulations also address some of the ways in which the name of a drug may render its labeling misleading.¹³ In addition, labeling is relevant to determining whether a drug is a new drug under section 201(p) of the FD&C Act (21 USC 321(p)), for which premarket approval is required (see sections 505(a) and 301(d) of the FD&C Act (21 U.S.C. 355(a) and 331(d)).

⁹ Smetzer, JL, and MR Cohen., 2007, The role of drug names in medication errors, in MR Cohen, Medication Errors, 2nd ed., Washington, DC: American Pharmacists Association, pp. 87-110.

¹⁰ 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 website at <https://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm145390.htm>.

¹¹ These performance goals and commitments were undertaken in connection with the authorization of the Biosimilar User Fee Act (BsUFA). For more information on FDA's BsUFA performance goals, see FDA's website at <https://www.fda.gov/industry/fda-user-fee-programs/biosimilar-user-fee-amendments>

¹² Labeling includes the prescribing information, container labels, carton labeling, and FDA-approved patient labeling.

¹³ See, e.g., 21 CFR 201.6(b), stating that labeling for a drug containing two or more ingredients may be misleading if the name of the drug designated in that labeling includes or suggests the name of one or more but not all of the ingredients; 21 CFR 201.10(c)(3), stating that labeling of a drug may be misleading if it employs a fanciful proprietary name for a drug or ingredient that implies some unique effectiveness or composition when the drug or ingredient is in fact a common substance, the limitations of which are readily recognized when the drug or ingredient is listed by its established name; 21 CFR 201.10(c)(5), stating that labeling of drug may be misleading if the proprietary name may be confused with the proprietary name or established name of a different drug or ingredient because of similarity in spelling or pronunciation.

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FDA reviews a proposed proprietary name as part of a prescription drug product's labeling through the application review process for the product.¹⁴ Although PDUFA and BsUFA performance goals provide for the Agency to make a tentative determination of acceptance or non-acceptance of a proposed proprietary name early in the review process (in instances where the proprietary name review request is submitted as a complete submission), final acceptance of a proposed proprietary name occurs as part of the approval of the drug product. Each name is evaluated on a case-by-case basis.

Sponsors have an ongoing obligation to ensure that each marketed product satisfies applicable requirements, such as ensuring that its labeling is not false or misleading in any particular (see section 502(a) of the FD&C Act). If a marketed product's proprietary name causes or contributes to medication errors, the sponsor of that product should work expeditiously with FDA to resolve the situation. If the product does not comply with applicable requirements and the sponsor is unwilling to address or resolve an issue voluntarily, the sponsor may be subject to enforcement actions.

The sections below outline considerations for developing and evaluating a proposed proprietary name, which are described in greater detail in this guidance. Sections III and IV focus on evaluating factors within the name or related to the naming strategy that are likely to contribute to medication errors. Section V provides our recommendations for evaluating the proposed proprietary name to help ensure compliance with FDA-administered statutory and regulatory provisions, and section VI describes our current thinking on evaluating the proposed proprietary names for look-alike and sound-alike risks.

For each category, we believe that no single test or standard is adequate to determine whether a proposed proprietary name may contribute to errors or otherwise contribute to any violation of the FD&C Act. Rather, the current approach to proposed proprietary name evaluation uses a combination of different and complementary tests.

III. PRESCREENING PROPOSED PROPRIETARY NAME FOR ATTRIBUTES THAT ARE LIKELY TO CONTRIBUTE TO MEDICATION ERRORS

This section identifies attributes of proposed human prescription drug product proprietary names that FDA typically finds concerning and that generally can be identified through prescreening by sponsors. We recommend that sponsors screen proposed proprietary names for the attributes described below as a first step before proceeding with a full assessment of whether a name is likely to contribute to medication errors or otherwise contribute to violations of the FD&C Act. We recommend that sponsors avoid proposed human prescription drug product proprietary names that raise concerns during preliminary screening. The sections below explain FDA's thinking on each of these aspects.

¹⁴ See FDA's guidance entitled "Contents of a Complete Submission for the Evaluation of Proprietary Names", dated April 2016, available at <https://www.fda.gov/media/72144/download>.

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A. Obvious Similarities in Spelling and Pronunciation of Proprietary Names

FDA recommends that sponsors avoid proposed proprietary names that are similar in spelling or pronunciation to existing proprietary names, established (or proper) names, or names of ingredients of other products. A drug's labeling may be misleading if its proprietary name is similar in spelling and/or pronunciation such that it may be confused with the proprietary name or the established name of a different drug or active ingredient (see § 201.10(c)(5) (21 CFR 201.10(c)(5))). FDA uses the Phonetic and Orthographic Computer Analysis (POCA) tool to determine the similarity between names as detailed in section VI.C. Research has shown that names involved in postmarketing medication errors generally have a higher degree of similarity.¹⁵ Based on this research and our postmarketing experience, names with high similarity scores are more likely to result in confusion. Generally, names that are nearly identical in spelling and/or pronunciation generate a similarity score of 70% or higher on the POCA tool.¹⁶

B. Inert or Inactive Ingredients

We recommend that proposed proprietary names not incorporate any reference to an inert or inactive ingredient (as defined in § 210.3(b)(8) (21 CFR 210.3(b)(8))), because doing so may create a misleading impression that the ingredient's value is greater than its true functional role in the formulation (see, e.g., § 201.10(c)(4)).

C. Combinations of Active Ingredients

FDA recommends against proprietary names of fixed combination drug products that include or suggest the name of one or more, but not all, of its **active ingredients** (as defined in § 210.3(b)(7)), because such names can mislead the end user by implying that the product contains only the ingredient or ingredients included in, or suggested by the name (see 21 CFR 201.6(b) and section 201(n) of the FD&C Act).

D. United States Adopted Name Stems

We recommend that sponsors avoid proprietary names that incorporate United States Adopted Name (USAN) stems in the position that USAN designates for the stem in a nonproprietary or established name. 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. Using these stems in the position designated by USAN within the proprietary names, when used inconsistently with the intended USAN meaning, may imply that a product has a pharmacological or chemical trait that it does not. Even when using these stems within the proprietary names is consistent with the USAN meaning, it can result in the creation of multiple similar proprietary names and/or proprietary names that are similar to the nonproprietary or established names for other drug

¹⁵ Lambert, BL, S-J Lin, K-Y Chang et al., 1999, Similarity as a risk factor in drug-name confusion errors: The look-alike (orthographic) and sound-alike (phonetic) model, *Medical Care*, 37(12):1214–1225.

¹⁶ POCA Program, available at <http://www.fda.gov/Drugs/ResourcesForYou/Industry/ucm400127.htm>.

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products, leading to an increased risk of medication errors. We recommend as best practice that sponsors screen proposed proprietary names against the stem list created by the USAN Council to ensure that a USAN stem is not present in the stem position in the proprietary name.¹⁷

However, FDA is less concerned about USAN stems that consist of two letters in proprietary names and would generally not object to their use. The two-letter stems are often not distinct enough to be recognized as USAN stems. Also, some two-letter stems are outdated and have not been used by the USAN Council for years. There are currently five stems that consist of two letters as identified by the USAN Council.¹⁸

Two-letter stems have very few associations and, in some cases, are rarely used (e.g., -ac last used by USAN Council in 1997 (nepafenac); -aj- only used once by USAN Council in 1976 for lorajmine). We also note that USAN has used some of the two-letter stems in established names (vortioxetine, afoxolaner), as well as included them in other stems (-tioxetine) that are inconsistent with the cited stem definition. This has resulted in conflicting stems, and therefore, in those instances, the stem does not support the USAN Council naming system or accurately indicate the pharmacological or chemical trait of the drug. Additionally, based on our postmarketing experience, the two-letter stems have not raised similar safety concerns that we have identified with longer stems.¹⁹

FDA generally would not object to the inclusion of letters found within a USAN stem but located within a position not reserved by USAN for the stem in a nonproprietary or established name, because this likely would not create the same degree of risk for confusion as those names that have the stem in the USAN-designated position.

In some cases, FDA may find a proposed proprietary name acceptable even if it includes a USAN stem in the USAN-designated position. 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,” using the letters “gest,” which are a USAN stem, is unavoidable.

E. Brand Name Extension

In this guidance, FDA uses the term **brand name extension** to refer to a naming strategy that uses a proprietary name that is already associated with one or more marketed drug products, with or without a **modifier**, for a product that *does not share any active ingredient(s) or active moiety(ies)* with the marketed product(s). Two examples of what FDA considers as brand name extensions are:

¹⁷ See the list of approved USAN stems, available at: <https://www.ama-assn.org/about/united-states-adopted-names/united-states-adopted-names-approved-stems>, last accessed 12/10/19

¹⁸ -ac: anti-inflammatory agents (acetic acid derivatives); -aj-: antiarrhythmics (ajmaline derivatives); ef-: Fc fusion protein; -fo-: phosphoro derivatives; and io-, -io-: iodine containing contrast media (accessed April 2, 2019).

¹⁹ Institute for Safe Medication Practices, 2003, Safety briefs: Aripiprazole or rabeprazole?, ISMP Med Saf Alert Acute Care, 8(8):1-3;

Institute for Safe Medication Practices, 2002, Safety Briefs, ISMP Med Saf Alert Acute Care, 7(17):1-2.

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1. The proprietary name “Drugname” is already associated with a marketed product that contains a specific active ingredient or active moiety, and the sponsor uses the same proprietary name “Drugname,” with or without a modifier, to introduce a new product that does not contain that same active ingredient or active moiety.
2. A sponsor uses a portion of the proprietary name already associated with a marketed drug product (e.g., the use of a shared **prefix** letter string with a modified **suffix** letter string, whereby the prefix letter string evokes the proprietary name already associated with a marketed drug product), with or without a modifier, to introduce a new product that does not contain the same active ingredient or active moiety.

FDA advises against using brand name extension to introduce a new product. 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.

In some cases, using the same proprietary name that is already associated with another marketed drug product has led to the use of a product for the wrong indication, in the wrong patient population, at the wrong dose, or in a contraindicated manner. Some of the errors caused by these types of name confusions have resulted in *serious adverse events* when patients were erroneously medicated with an active moiety that was not intended to be administered.

F. Reuse of Proprietary Names

FDA recommends that sponsors refrain from using the proprietary name of a product that is no longer marketed to name a different drug product, because there is a strong risk that end users may continue to associate the name with the original discontinued product. Prescribers often continue to use the proprietary name of discontinued products. For example, when prescribing a drug for which there are marketed generics, prescribers may refer to the proprietary name of the discontinued brand version.²⁰ Proprietary names associated with discontinued drug products also may continue to appear in drug product reference texts and electronic media for extended periods of time.

If proprietary names are proposed for reuse, FDA will assess them on a case-by-case basis, considering factors that might establish the drug name familiarity, including length and extent of product distribution, the existence (or lack thereof) of past or current generic equivalents, and data that might otherwise show health care professional familiarity with the drug name. If a sponsor chooses to use this approach in naming, we recommend sponsors consider the above factors and provide data to support that reusing the proprietary name of a discontinued product will not be problematic.

Note that in its evaluation of the proposed proprietary name for a new product, FDA does not consider a proposed name to be “reused” if it is one that FDA previously found acceptable for a

²⁰ 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

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different product, but that was never used to market that earlier product. If submitted anew, FDA will evaluate the acceptability of the name for the new product.

G. Use of Letters and Numbers That Are Unpronounceable as a Word in Proprietary Names

Generally, as a best practice, proprietary names should be pronounceable as a word because proprietary names are used by health care professionals when prescribing, ordering, transcribing, dispensing, and administering drugs, and when counseling patients on their medications. We discourage sponsors from proposing proprietary names that consist of a mixture of letters or numbers placed together (e.g., IVS458). Such names may not be understood as drug names that are typically composed of letters only, or they could be misconstrued as another element associated with the drug product or prescription, such as dose or route of administration. Names constructed in this manner could lead to medication errors depending on the nature of the misinterpretation.

IV. ADDITIONAL BEST PRACTICES FOR EVALUATION OF PROPOSED PROPRIETARY NAME

In addition to the preliminary screening recommendations described in section III, we recommend that sponsors consider other important attributes described in this section during name development and before proceeding with further assessment to reduce the likelihood that a prescription drug's proprietary name will contribute to medication errors or other violations of the FD&C Act and its implementing regulations, either at the time of initial product launch or in the event of future product development. FDA intends to evaluate each proposed proprietary name for these attributes and determine its acceptability on a case-specific basis.

A. Names That Include Reference to Product-Specific Attributes

For flexibility in future product development and naming, FDA recommends that sponsors avoid incorporating product-specific attributes, such as manufacturing characteristics (e.g., "NameLyophilized"), dosage form (e.g., "Nametabs") or route of administration (e.g., "Nameoral"), as part of the proposed **root proprietary name**. It is not uncommon for product-specific attributes to change during a drug's life cycle with subsequent introductions of new dosing intervals, formulations, dosage forms, indications, and patient populations. If considering a proprietary name that includes or refers to product-specific attributes, sponsors should be mindful that future changes, such as changes in dosage form or route of administration, could render the root proprietary name inaccurate and thus unusable for future formulations.

If references to product-specific attributes are included in the root proprietary name, FDA recommends that the name be evaluated to ensure that the product-specific attribute is consistent with the terminology used in the product's labeling and does not pose risks for medication error.

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B. Medical Abbreviations

Sponsors are generally discouraged from incorporating symbols, dose designations, and medical abbreviations commonly used for prescription communication in their proposed proprietary name because their inclusion could inadvertently introduce a source of error.

We recommend consulting 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 when considering the risk that a proposed proprietary name incorporating an abbreviation, symbol, or dose designation in a proposed proprietary name will be subject to misinterpretation.^{21,22}

When evaluating a proposed proprietary name that contains an element that is also an abbreviation, symbol, or dose designation, FDA recommends considering other factors such as placement and presentation that may influence interpretation of the element to make sure the way it is presented in the name is not error-prone. As an example, "po" has been used historically as an abbreviation for oral route of administration in a medication order, typically appearing after the drug name. Therefore, while the inclusion of letters "po" in the beginning or within the root proprietary name (e.g. Poname or Napome) is unlikely to be misconstrued as a medical abbreviation, and thus would not be expected to pose a risk for medication errors, if "po" is used in the ending of the root proprietary name or as a modifier (e.g. Name PO or Namepo), this would increase the likelihood of "po" being misconstrued as an abbreviation for the oral route of administration and thus create confusion if this is not the intended meaning.

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 generally consists of one or more letters, symbols, numbers, and/or words, and appears at the beginning or end of the root proprietary name, typically set off by a space or hyphen. Sponsors frequently propose a shared root proprietary name with various modifiers to distinguish among multiple products that contain at least one shared active ingredient.

Inconsistencies in the use of modifiers and the absence of a standardized meaning for some modifiers that are meant to convey information about a product have been a source of confusion to end users.^{23,24,25} For example, sometimes modifiers are used to convey distinguishing product

²¹ The Joint Commission's Official "Do Not Use" List of Abbreviations, 2004, available at http://www.jointcommission.org/assets/1/18/Official_Do_Not_Use_List_6_111.PDF, last accessed 12/10/19

²² The Institute for Safe Medication Practices' (ISMP) List of Error-Prone Abbreviations, Symbols, and Dose Designations, 2017, Horsham (PA), available at <http://www.ismp.org/tools/errorproneabbreviations.pdf>, last accessed 12/10/19

²³ Pennsylvania Patient Safety Authority. Drug Name Suffix Confusion is a Common Source of Errors. 2004 Dec;1(4):17-8

²⁴ Institute for Safe Medication Practices. ISMP Medication Safety Alert! 2003 Oct;(8)21

²⁵ Institute for Safe Medication Practices. ISMP Medication Safety Alert! 2003 Oct;(8)21

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characteristics, such as “Name ODT” (an orally disintegrating tablet) or “Name XR” (an extended-release formulation). Confusion stemming from the use of modifiers in proprietary names has led to medication errors, such as dispensing and administering 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 such risks, FDA encourages sponsors that choose to use modifiers to select, whenever possible, an existing modifier with an established meaning that has not been a source of confusion (see Appendix A for examples of modifiers that, when intended to express the accompanying meaning, have not been a source of confusion).

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

1. General Considerations When Developing a Proprietary Name That May Include a Modifier

- Do you currently market one or more products under the proposed **root proprietary name**?
 - Proprietary names for prescription products that involve the use of *family trade names* are evaluated on a case-by-case basis. Each request for review of a proposed proprietary name that includes a family trade name will be evaluated to consider whether the:
 - i. Products share at least one active ingredient or active moiety
 - ii. Products are differentiated by labeling (carton and container)
 - iii. Modifier conveys accurate information about the product
 - iv. Modifier effectively differentiates the product from other products in the product line

In some cases, this naming practice has posed problems when the same root name is used for multiple products without modifiers that adequately differentiate the products.²⁶ The types of errors that have resulted from family trade name confusion include, for example, 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.

- Does the product have a characteristic (e.g., extended-release formulation) that is typically described by a modifier for other products that share that same characteristic?

²⁶ Institute for Safe Medication Practices, 2004, Safety Briefs: Caution: Dulcolax brand name extensions, ISMP Med Saf Alert Acute Care, 9(7):1-2.

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In certain instances, a modifier associated with specific characteristics (such as XR for extended-release formulations or ODT for orally disintegrating tablets) may be beneficial even if no product with these characteristics is marketed under the same root proprietary name. For example, there may be other immediate-release formulations containing the active ingredient that are marketed under different root names. In these cases, the addition of a modifier may provide incremental benefit in signaling the correct route or manner of administration.

- Where will the modifier be placed in relation to the root proprietary name? Are there any conventions for the modifier placement that are used within the particular drug product class?
 - Although modifiers are usually placed at the end of the root name, there may be certain instances in which the modifier is placed at the beginning of the root name. For example, proprietary names of oral contraceptives often include modifiers before the root name, such as Lo Simpess, Tri-Linyah. In these cases, the placement of modifiers is consistent with the established proprietary naming practices for the class.
- What is the risk of medication error resulting from omitting a modifier or alternatively including a modifier that is misinterpreted as a medical term, abbreviation, or other medical product name?²⁷
 - In some instances, analysis of the risk of errors related to the use of a modifier may suggest that the use of an entirely distinct proprietary name for a product is safer than the use of the same root proprietary name with a modifier (see section IV.D for a detailed discussion of the risks). Such circumstances may arise when a product under development will have significantly different indications and usage, patient populations, dosages, safety profiles, or routes of administration from the marketed product.

2. Additional and Special Considerations Related to Certain Types of Modifiers

In addition to the above general considerations that are applicable to all modifier assessments, there are certain types of modifiers that are commonly used and warrant special considerations as described below.

a. Descriptive modifiers

Some modifiers are composed of letters or words that are meant to convey information about the product's composition or use, and FDA refers to these as descriptive modifiers. Examples would include the abbreviations in Appendix A and accompanying words to

²⁷ See section VI for consideration on how to identify names with potential similarity to the proposed modifier.

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describe some aspect of the product (e.g., indication, formulation, patient population). For example, the modifier “viscous” in Photrexa Viscous describes the formulation.

Potential for medication errors arises when descriptive modifiers are ambiguous, misleading, or subject to misinterpretation. A primary factor in evaluating a modifier associated with a proprietary name is whether the modifier’s intended meaning is supported by the labeling and whether it is understood by the end user. Some factors to consider are:

- If the modifier is intended to convey information about a pertinent characteristic of the product, does it accurately describe that characteristic?
- What is the modifier’s intended meaning? Are there data from a label comprehension study (or similar study) or data available from published literature to support that health care professionals and consumers understand the intended meaning?
- What is the risk if end users misinterpret the modifier’s intended meaning? What is the impact of a medication error if an end user confuses the modifier with some other element of a prescription or order (such as frequency, strength, route of administration)? Alternatively, what is the risk if the modifier is omitted?
- Is the proposed modifier currently used in the marketplace? We recommend checking the ISMP’s current List of Products with Drug Name Suffixes and other drug information references to determine whether the proposed modifier is already used in the marketplace and whether it has been used consistently with a commonly recognized meaning.²⁸ If an existing modifier with the same intended meaning is in the marketplace and familiar to and understood by end users without error, FDA recommends adopting that existing modifier. When deciding whether to use a different modifier instead of an existing modifier with the same intended meaning, consider whether the proposed modifier conveys the intended meaning as clearly as, or more clearly than, the existing modifier.

b. Combination drug-device product modifiers

Some proprietary name modifiers represent the delivery device component of a combination drug-device product. When the device component name is presented contiguously with the drug component name and is part of the proposed proprietary name, such modifiers are reviewed as part of the Center for Drug Evaluation and Research’s (CDER’s) or the Center for Biologics Evaluation and Research’s (CBER’s) proprietary name evaluation. Conventionally, for drug-device products with a drug primary mode of action, the proprietary name of the drug component precedes the proprietary name or modifier of the device component. For example, a product integrating a drug and a disposable injector device might use a name such as “Drugname Pen,” composed of the root proprietary name for the drug component followed by the

²⁸ ISMP’s List of Products With Drug Name Suffixes internet, 2010. Horsham (PA): Institute for Safe Medication Practices, available at <http://www.ismp.org/Tools/drugnamesuffixes.pdf>, last accessed 12/10/19

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modifier “pen” indicating the presence of the device component. Generally, modifiers used with combination products that represent a device component are either (a) a descriptive modifier that conveys the type of device such as “Pen,” “Prefilled Syringe,” or “Inhaler” or (b) a sponsor-coined modifier, such as “SOLOSTAR” or “Diskus.”

A descriptive modifier may be suitable to use across different combination products provided it accurately describes the combination product. Such descriptive modifiers tend to convey in a general manner the category or type of device component (e.g., “Pen,” “Prefilled Syringe,” “Inhaler”). Although the device constituent part across various combination products that use the same descriptive modifier may operate differently and may contain different drugs, if the descriptive modifier is well understood as describing a general category or type of device component to end users, FDA would generally not have concern for confusion or errors.

Conversely, a sponsor-coined modifier may be well understood to represent a specific device platform or technology. For these types of modifiers, sponsors may wish to use the same modifier for a specific device platform across a number of drug-device combination products, each containing different active moieties, to help prescribers and end users understand the similar nature of the products. In such situations, FDA generally will not object to this naming strategy if the drug component portions of the proprietary names are adequately distinguishable and any differences in the operation of the device across products is minor and otherwise not expected to result in errors.²⁹

A final consideration for device modifiers used with drug-device combination products relates to the introduction of a new device component that operates similarly, but not identically, to a previously marketed device component that delivered the same drug product. For example, if a sponsor is developing a drug-device combination product that includes a new disposable injector device which introduces differences in critical tasks that are likely to result in errors among prior users compared to an earlier marketed device,³⁰ a distinct modifier should be used to represent the new combination product in order to communicate to prescribers and patients that the new combination product operates differently from the earlier marketed combination product.

c. Use of numbers and symbols in modifiers

FDA generally recommends sponsors avoid the use of numbers within a proprietary name. Both Roman and Arabic numbers have been mistaken for the strength, quantity,

²⁹ It is likely that FDA would have concern with the use of a single sponsor-coined modifier across combination products that do not operate similarly because it may mislead users and potentially lead to errors when administering the product.

³⁰ Critical tasks are those tasks that users must perform to safely and correctly use the product.

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duration, or controlled substance class of prescription drug products.^{31,32} For example, when a drug order or prescription is written for a drug product with a proprietary name that has the number “3” (to represent product strength) as part of its name, this might be misinterpreted to mean that *three* tablets are to be dispensed or that the product should be used for only 3 days. FDA also generally recommends against using symbols (e.g., “+” or “&”) as part of proprietary names because symbols can be misinterpreted, misread, or confused (e.g., “+” could be read as “4”).³³ Therefore, as a best practice, FDA recommends using words rather than symbols.

There are a few classes of drugs, however, for which there has been a historical practice of using a slash (/) or hyphen (-), or of using numbers as modifiers, resulting in established proprietary naming conventions for that class of drugs. In these cases, FDA does not generally expect to object to proprietary names that include use of these elements that are consistent with the established practice for the class. For example, the proprietary names of oral contraceptives may include the use of a slash or hyphen (Tri-lynah, Junel 1/20) or vaccines may include the valency (Myvaccine 10). There may be a few instances where the use of numbers as modifiers minimizes the risk of errors and promotes appropriate use of the products by conveying information to end users. For example, the proprietary names of oral contraceptives often include numerical modifiers to help differentiate among various strengths of the products. Similarly, the proprietary names of insulin mixtures may use numerical modifiers to represent the proportion of each type of insulin in the mixture.

D. Dual Proprietary Names

In certain cases, a modifier may not effectively convey a characteristic of the proposed product or reliably differentiate the proposed product from other products that contain the identical active moiety or ingredient(s). Such circumstances may arise when a product under development will have significantly different indications and usage, patient populations, dosages, safety profiles, or routes of administration from the marketed product. For example, two products may be administered using different routes of administration, or have differing doses, which may present a risk of medication errors to a population taking the product for a second indication. In these unique instances, the use of two different proprietary names (also referred to as dual proprietary name) may be a safer naming approach. However, sponsors should also consider the risks associated with this naming strategy. For example, practitioners may be unaware that two products with different proprietary names prescribed for concomitant use contain the same active ingredient. This could lead to overdose or dose-related adverse events. Another risk may be if a drug-drug interaction is not noted because the health care professional and patient are unaware that a product sold under one proprietary name contains the same active ingredient as another

³¹ Institute for Safe Medication Practices. Misidentification of alphanumeric characters. ISMP Medication Safety Alert! Community/Ambulatory Care Edition. 2014 Jun; (19)11. <https://www.ismp.org/resources/misidentification-alphanumeric-symbols>, accessed 1/13/20.

³² Institute for Safe Medication Practices. ISMP Medication Safety Alert! 2002 Jun; (7)13.

³³ ISMP’s List of Error-Prone Abbreviations, 2010, Symbols, and Dose Designations. Horsham (PA): Institute for Safe Medication Practices, available at: <http://www.ismp.org/tools/errorproneabbreviations.pdf>, last accessed 12/10/19

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product with a different proprietary name. Sponsors should assess the safest naming convention for their situation and develop labeling and other measures to mitigate the risks associated with dual proprietary names. FDA will evaluate these proposals on a case-specific basis along with any associated labeling that might address these potential risks.

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

Medication errors resulting in dispensing and administering the wrong drug can occur when a proprietary name for a product marketed in the United States is identical, or nearly identical in spelling and pronunciation, to the proprietary name of a foreign product containing an entirely different active ingredient marketed only in a foreign country. As seen in the example reported by ISMP, a medication error occurred when a patient took digoxin instead of the intended diltiazem product, both of which were marketed under the same proprietary name, Dilacor, in different countries.³⁴ For this reason, as a best practice, FDA recommends 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 (and even if the foreign product is not marketed in the United States).

F. Incorporation of the Sponsor's Name

FDA recommends that sponsors avoid proposed proprietary names that incorporate the sponsor's name, or some part of the sponsor's name, across multiple products (e.g., "ABCName1," "ABCName2," "ABCName3"). This practice results in creating multiple similar proprietary names, increasing the risk of confusion among the products. The practice could pose safety risks when products are stored alphabetically in distributor or pharmacy locations or when products are ordered from alphabetized lists.

V. FURTHER BEST PRACTICES FOR REVIEW, INCLUDING FOR MISBRANDING AND OTHER LEGAL CONCERNS

Although this guidance focuses primarily on aspects of proprietary names that can contribute to medication error, as a best practice, sponsors should avoid using a proprietary name that could contribute to any violation of the FD&C Act. For example, among other things, the FD&C Act provides that a drug is misbranded if its labeling is false or misleading in any particular (section 502(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 instance, a fanciful proprietary name may misbrand a product by suggesting that it has some unique effectiveness or composition when it is actually a common substance, the limitations of which are readily recognized when the product is listed by its established name (see § 201.10(c)(3)). For example, a proposed proprietary name that contains *cure* or that sounds like *cure* for a drug that treats the symptoms associated with a chronic disease would be concerning.

³⁴ Institute for Safe Medication Practices, 2005, Safety briefs: Same name, different drug, ISMP Med Saf Alert Acute Care, 10(1):2

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The word “cure” is defined as “something (such as a drug or medical treatment) that stops a disease and makes someone healthy again” or “something that ends a problem or improves a bad situation.”³⁵ Therefore, if a proposed proprietary name for a chronic disease contains or sounds like “cure,” it would overstate the clinical benefit by misleadingly implying that the product can *cure* the chronic condition. As another example, a drug is a new drug if it is not generally recognized as safe and effective (GRASE) for use under the conditions prescribed, recommended, or suggested in its labeling (section 201(p) of the FD&C Act), and the introduction of a new drug into interstate commerce without an approved application is prohibited (sections 301(d) and 505(a) of the FD&C Act; see also section 351 of the PHS Act). If the proprietary name of a drug suggests that it be used under conditions for which it is not GRASE and for which it does not have an approved new drug application (NDA) or biologics license application (BLA), distributing that drug with labeling bearing that proprietary name would violate the FD&C Act.

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.³⁶ Research has shown that linguistic characteristics can influence the way people perceive a product, particularly when it is new and unfamiliar as is the case with newly proposed proprietary names.³⁷

If a sponsor chooses to review for concerns other than those likely to contribute to medication errors, FDA recommends such a review be performed independent from a medication error review to minimize bias in either review. The review should focus on identifying names that overstate product efficacy or safety, expand product indications, suggest superiority without substantiation, or are of a fanciful nature that misleadingly implies unique effectiveness or composition. The analysis of sound empirical data, if available, should be given prominence in evaluating proposed proprietary names.

One possible study methodology and some sample questions are outlined in Appendix B. These sample questions are designed to guide sponsors in the development of outcome measures in their studies but are not intended to be an exhaustive list. Sponsors are encouraged, but not required, to seek advisory comments from the Agency on their proposed study methodology, questionnaire, and analysis plan before collecting data.

³⁵ “Cure,” *Merriam-Webster.com* (available at <https://www.merriam-webster.com/dictionary/cure>; accessed April 3, 2019).

³⁶ Bergen, B.K., 2004. The psychological reality of phonaesthemes, *Language*, 80:290-311.

³⁷ Lowrey, TM, LJ Shrum, and TM Dubitsky, 2003, The relation between brand name linguistic characteristics and brand name memory, *Journal of Advertising*, 32:7-17. See also Keller, KL, SE Heckler, and MJ Houston, 1998, The effects of brand name suggestiveness on advertising recall, *Journal of Marketing*, 62:48-57. These researchers, for example, conducted an experiment to investigate whether names that were suggestive of a particular characteristic of the product increased the recall and therefore the success of the communication. They found that participants better recalled suggestive names for characteristics relevant to the product (e.g., a television’s picture quality; PicturePerfect) than those that were not suggestive (e.g., Emporium). Other researchers have found that even parts of words or phonemes can influence perceptions and consumer judgments about unfamiliar names (Klink, RR, 2000, *Creating brand names with meaning: The use of sound symbolism*, *Marketing Letters*, 11:5-20; Yorkston, E and G Menon, 2004, A sound idea: Phonetic effects of brand names on consumer judgments, *Journal of Consumer Research*, 31:43-51).

VI. RECOMMENDED METHODS FOR EVALUATING RISKS OF MEDICATION ERROR POSED BY SIMILARITY OF A PROPOSED PROPRIETARY NAME TO OTHER NAMES

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

Specific methods that FDA uses to evaluate proposed proprietary names, as well as methods that FDA recommends sponsors use before submitting a proposed proprietary name for FDA review, are described below. The descriptions include methods for identifying existing proprietary names or established names that could be confused with a sponsor's proposed name, as well as methods for assessing the likelihood and potential effects of name-related medication errors. If a sponsor includes detailed study report(s) providing data from its own safety assessment(s) and shows that these data were generated using a methodology that is generally consistent with that described in this guidance, FDA intends to use these data to help evaluate the risk that the proposed proprietary name would contribute to medication errors. Sponsors are encouraged to conduct each of the types of assessments described below, but FDA considers what is submitted on its individual merits, regardless of whether the assessment includes every type of testing described below.³⁸

A. Name Simulation Studies

Name simulation studies conducted by FDA test how health care professionals employed by FDA respond to the proposed names. The studies we conduct are limited in scope because they involve only FDA staff. Although the sample size in FDA's simulation studies is small, these studies can provide important qualitative data that can be used to identify the potential vulnerability of a proposed name to be misinterpreted. The likelihood of observing an error in a small study is low, so that when an error is observed in a small study, this suggests that there will be errors in actual use. However, small studies may not be sufficiently sensitive to reliably identify all risks associated with a proposed proprietary name; the absence of observed errors in small studies is not conclusive evidence that a proposed name will not be confused with another

³⁸ Because sponsors do not have access to non-public information on pending proposed proprietary names, FDA generally intends to use the methods described in this guidance to generate data to supplement any safety assessments provided by sponsors using the methods described in section VI to evaluate the proposed proprietary name for its potential to be confused with any non-public pending proposed proprietary names. FDA may use the data identified from this supplementary evaluation of pending proposed name to determine if there are two or more proprietary names under review that could result in medication errors caused by potential confusion with each other. In these instances, FDA will notify both applicants of the conflict.

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drug product's proprietary name. For these reasons, FDA believes it would be useful for sponsors to conduct more comprehensive simulation studies.

Appendix C outlines elements that are recommended for consideration if sponsors choose to conduct simulation studies.

B. Obtain Medication Error Data for Names That Are Already Associated With Marketed Products

Case reports of medication errors related to proprietary names that are already associated with marketed products can help inform the analysis of a proposed proprietary name. FDA monitors medication error reports to identify cases of name confusion with the goal of identifying relevant information about the causes of problems and failures that lead to medication error, and the Agency applies any relevant information to the evaluation of a proposed proprietary name. FDA recommends that sponsors obtain medication error report information from their internal safety databases, publicly available VAERS (Vaccine Adverse Event Reporting System) or FAERS (FDA Adverse Event Reporting System) data,³⁹ published literature, and resources available through patient safety organizations such as ISMP.

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, proper, and/or proposed proprietary name that may be relevant to using the proposed proprietary name in the United States, FDA recommends this information be provided to FDA in the proprietary name submission.⁴⁰

C. Computational Method To Identify Names With Potential Orthographic, Spelling, and Phonetic Similarities

FDA evaluates the orthographic and phonetic similarity of a proposed proprietary name to other names by using the POCA software.⁴¹ FDA enters the proposed proprietary name into FDA's POCA system and queries the proposed proprietary name against names in drug reference databases (e.g., Drugs@FDA and RxNorm). Sponsors may include a POCA evaluation with their proprietary name submissions; when included, FDA will use data from a sponsor's POCA evaluation to help evaluate the proposed proprietary name, provided that the methodology employed to generate the data is generally consistent with the methods described below.

³⁹ Available at

<https://www.fda.gov/drugs/guidancecomplianceregulatoryinformation/surveillance/adversedruggedeffects>.

⁴⁰ See 21 CFR 312.32(b). Sponsors are required to promptly review all information relevant to the safety of the drug product obtained or otherwise received from any source, foreign or domestic, including information derived from any clinical or epidemiological investigations, reports in the scientific literature, unpublished scientific papers, reports from foreign regulatory authorities, and reports of foreign commercial marketing experience for drugs that are not marketed in the United States.

⁴¹ On February 17, 2009 (74 FR 7450), FDA announced the availability of the source code and supporting technical documentation for POCA software program royalty-free to the public.

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Regardless of whether a sponsor submits data from POCA for FDA to consider in its review, FDA will independently conduct a review using POCA to 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 the names of pending products that are not publicly known to other sponsors proposing proprietary names.⁴²

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

The threshold FDA uses to conduct the orthographic and phonetic searches is set at a combined score of 55%, based on the validation work done on the POCA algorithms. Based on our postmarketing experience, the combined measure of similarity has been positively correlated to errors involving name confusion.

When using POCA, 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.⁴³

The POCA search will provide three data sets: (1) COMBINED orthographic and phonetic matches, (2) phonetic matches, and (3) orthographic matches. Sponsors should review the COMBINED orthographic and phonetic matches and group the name pairs into one of the following three categories:

- Highly Similar Name Pair: combined match percentage score $\geq 70\%$
- Moderately Similar Name Pair: combined match percentage score $\geq 55\%$ to $\leq 69\%$
- Low Similarity Name Pair: combined match percentage score $\leq 54\%$

As a general principle, the higher the percentage assigned by POCA, the greater similarity the proposed proprietary name has to the name identified by POCA. Research has shown that names involved in postmarketing medication errors because of prescribing or dispensing the wrong drug have a higher degree of similarity than drug names that were not involved in these types of

⁴² Proposed names may be associated with drug products related to investigational new drug applications, NDAs, biologics license applications, or abbreviated new drug applications. In those rare instances when a conflict is identified with the proposed proprietary names of two pending drug applications, FDA will notify both Applicants of the conflict in accordance with the Manual of Policies and Procedures: Procedures for Sharing Non-public Information on Pending Proposed Proprietary Names, which is available at: <http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ManualofPoliciesProcedures/UCM521551.pdf>.

⁴³ FDA only searches the combined root name and modifier in POCA if the total length of the name (root name + modifier) is 10 letters or fewer. For modifiers located prior to the root name, e.g. Lo Ovral, Tri Sprintec, the entire name is searched in POCA.

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medication errors.⁴⁴ This research is corroborated by our postmarket surveillance of medication errors and root cause analyses. Therefore, based on this research and postmarketing surveillance, we expect names with high similarity scores to be more likely to result in confusion.

D. 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 Name Pair, Moderately Similar Name Pair, and Low Similarity Name Pair) described in section VI.C. The intent of these checklists is 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. Each bullet below corresponds to the name similarity category described in section VI.C. and cross-references the respective Appendix that addresses criteria that FDA uses to determine whether and to what extent a name presents a safety concern.

- For highly similar name pairs, based on postmarketing experience, we know that differences in product characteristics, including differences such as strength and dose, often cannot mitigate the risk of a medication error. Therefore, proprietary name pairs that are highly similar (i.e. have a combined score of $\geq 70\%$) are at greater risk for a look-alike and sound-alike confusion,⁴⁵ which is an area of concern for FDA (see Appendix D).
- Moderately similar name pairs should be further evaluated to identify the presence of attributes that are known to cause name confusion.
 - *Name attributes*: The first part of the drug name plays a significant role in contributing to name confusion. Additionally, drug name pairs that start with the same first letter and contain a shared letter string of at least 3 letters in both names are a major contributing factor in the confusion of drug names.⁴⁶ We evaluate all moderately similar name pairs retrieved from POCA to identify the above attributes. These name pairs are further evaluated to identify overlapping or similar strengths or doses.
 - *Product attributes*: Moderately similar name pairs of products that have overlapping or similar strengths or doses represent an area of concern to FDA. The dose and strength information is often located in close proximity to the drug name on prescriptions and medication orders, and that information can be an important factor that either increases or decreases the potential for confusion

⁴⁴ Lambert, BL, S-J Lin, K-Y Chang et al., 1999, Similarity as a risk factor in drug-name confusion errors: The look-alike (orthographic) and sound-alike (phonetic) model, *Medical Care*, 37(12):1214–1225.

⁴⁵ We have also identified similar concerns with individual orthographic or phonetic POCA scores of $\geq 70\%$.

⁴⁶ Shah, MB, L Merchant, IZ Chan et al., Characteristics that may help in the identification of potentially confusing proprietary drug names, *Therapeutic Innovation and Regulatory Science*, 51(2): September 2016.

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between similarly drug-named pairs. The ability of other product characteristics to mitigate confusion (e.g., route of administration, frequency of administration, dosage form) may be limited when the strength or dose overlaps. FDA will review such name pairs further to determine whether sufficient differences exist to prevent confusion (see Appendix E).

- Name pairs with low similarity are generally acceptable (see Appendix F) unless there are data to suggest that the name might be vulnerable to confusion (e.g., name simulation study suggests that the proposed proprietary name is likely to be misinterpreted as that of a marketed product). In these instances, we would reassign a low similarity name to the moderately similarity category and review accordingly (see Appendix E).

In conclusion, FDA's recommendations in this guidance are intended to help sponsors avoid choosing a proprietary name that is likely to contribute to medication errors or otherwise contribute to violations of the FD&C Act. In evaluating a proposed proprietary name, FDA considers the information and analyses about the proposed proprietary name described in this guidance, along with any additional name-related information submitted by the sponsor. Assessments of a proprietary name are necessarily fact-specific, and therefore, FDA's determinations are made on a case-by-case basis, considering the totality of the information.

GLOSSARY

The following terms are described only to assist in understanding how they are used in this guidance, and are not intended for use outside the context of this guidance:

Active ingredient: An *active ingredient* is any component that is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of the body of man or other animals. The term includes those components that may undergo chemical change in the manufacture of the drug product and be present in the drug product in a modified form intended to furnish the specified activity or effect. *See also* 21 CFR 314.3(b).

Active moiety: An *active moiety* means the molecule or ion, excluding those appended portions of the molecule that cause the drug to be an ester, salt (including a salt with hydrogen or coordination bonds), or other noncovalent derivative (such as a complex, chelate, or clathrate) of the molecule, responsible for the physiological or pharmacological action of the drug substance. *See also* 21 CFR 314.3(b).

Adverse reaction: An *adverse reaction* is an undesirable effect, reasonably associated with use of a drug, that may occur as part of the pharmacological action of the drug or may be unpredictable in its occurrence. *See also* 21 CFR 201.57(c)(7).

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: FDA uses the term *brand name extension* to refer to a naming practice that uses a **proprietary name** that is already associated with one or more marketed drug products, with or without a **modifier**, for a product that does not share any active ingredient(s) or active moiety(ies) with the marketed product(s).

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, prescribing physician, nurse, pharmacist, pharmacy technician, and other individuals who are involved in routinely procuring, stocking, storing, prescribing, dispensing, and administering medications (e.g., medication technicians).

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

48
49 the term “established name,” with respect to a drug or ingredient thereof, means (A) the
50 applicable official name designated pursuant to section 508, or (B) if there is no such
51 name and such drug, or such ingredient, is an article recognized in an **official**
52 **compendium**, then the official title thereof in such compendium, or (C) if neither clause
53 (A) or clause (B) of this subparagraph applies, then the common or usual name, if any of
54 such drug or such ingredient, except that where clause (B) of this subparagraph applies to
55 an article recognized in the United States Pharmacopeia and in the Homeopathic
56 Pharmacopoeia under different official titles, the official title used in the United States
57 Pharmacopeia shall apply unless it is labeled and offered for sale as a homeopathic drug,
58 in which case the official title used in the Homeopathic Pharmacopoeia shall apply.
59 [emphasis added]
60

61 **Family trade name:** A *family trade name* results from a naming practice involving the use of a
62 shared **proprietary name** to market multiple products with a shared active ingredient, using a
63 **suffix** or **modifier**, to distinguish the products from one another. This practice is also referred to
64 as *family branding*.
65

66 **Infix:** An *infix* is a group of letters that appears in the middle of the proprietary name.
67

68 **Label:** As defined in section 201(k) of the FD&C Act (21 U.S.C. 321(k)), the term *label* means
69 “a display of written, printed, or graphic matter upon the immediate container of any article.” If
70 any word, statement, or other information is required by the FD&C Act to appear on the label, it
71 must appear on the outside container or wrapper, if there is one, or be “easily legible through the
72 outside container or wrapper.”
73

74 **Labeling:** As defined in section 201(m) of the FD&C Act, the term *labeling* means “all labels
75 and other written, printed, or graphic matter (1) upon any article or any of its containers or
76 wrappers, or (2) accompanying such article.”
77

78 **Medication error:** A *medication error* is any preventable event that may cause or lead
79 to inappropriate medication use or medication-related patient harm while the medication
80 is in the control of the healthcare professional, patient, or consumer. Such events may be
81 related to professional practice, health care products, procedures, and systems, including
82 prescribing, order communication, product labeling, packaging, and nomenclature,
83 compounding, dispensing, distribution, administration, education, monitoring, and use.⁴⁷
84

85 **Modifier:** A *modifier* is a portion of the proprietary name. Some proprietary drug names are
86 constructed of a root proprietary name and added word(s) or other components that are referred
87 to as the modifier portion of the proprietary drug name. The modifier portion of a proprietary
88 drug name might be a letter, number, word, device name, or combination of letters, numbers, and
89 words appearing at the beginning or end of a root proprietary name, typically set off by a space
90 or hyphen.
91

⁴⁷ See also National Coordinating Council for Medication Error Reporting and Prevention, available at <https://www.nccmerp.org/about-medication-errors>, last accessed on May 19, 2020

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92 **Official compendium:** The term *official compendium* is defined in section 201(j) of the FD&C
93 Act as “the official United States Pharmacopeia, official Homeopathic Pharmacopoeia of the
94 United States, official National Formulary, or any supplement to any of them.”
95

96 **Packaging:** A *package* or *market package* refers to the **container closure system** and labeling,
97 associated components (e.g., dosing cups, droppers, spoons), and external packaging (e.g.,
98 cartons or shrink wrap). A *market package* is the article provided to a pharmacist or retail
99 customer upon purchase and does not include packaging used solely for shipping such articles.
100

101 **Prefix:** A *prefix* is a group of letters that appears at the beginning of the proprietary name.
102

103 **Proper name:** For biological products, the term *proper name* means the nonproprietary name
104 designated by FDA in the license for a biological product licensed under the PHS Act. *See also*
105 21 CFR 600.3(k).
106

107 **Proprietary name:** The *proprietary name* of a drug product is its brand name⁴⁸
108

109 **Root proprietary name:** Some proprietary names are constructed of multiple components.
110 When a proprietary name contains a modifier as one of the components, the non-modifier portion
111 of the proprietary name is referred to as the *root proprietary name*. The *root proprietary name*
112 may be shared by multiple products. An example of a *root proprietary name* for a prescription
113 drug product is Lantus in Lantus Solostar.
114

115 **Serious adverse event:** A *serious adverse event* is defined as an event that does or has the
116 potential to result in death, hospitalization, congenital abnormality, permanent disability, or
117 could be life-threatening. *See also* 21 CFR 314.80.
118

119 **Suffix:** A *suffix* is a group of letters that appears at the end of the proprietary name.
120

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

⁴⁸ Sometimes referred to as the product’s “trade name”

Databases and Other Resources

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

FDA Adverse Event Reporting System (FAERS)

FAERS is a database that contains adverse event reports and medication error reports submitted to FDA. The database is designed to support FDA’s postmarket safety surveillance program for drug and therapeutic biologic products. The informatic structure of the FAERS database adheres to the international safety reporting guidance issued by the International Council for Harmonization. Adverse events and medication errors are coded using terms in the Medical Dictionary for Regulatory Activities (MedDRA) terminology. More information about FAERS can be found at <https://www.fda.gov/drugs/surveillance/fda-adverse-event-reporting-system-faers>.

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 website provides a nationwide mechanism by which adverse events following immunization can be reported, analyzed, and made available to the public. The VAERS website also provides a vehicle for disseminating vaccine safety-related information to parents or guardians, health care professionals, vaccine manufacturers, state vaccine programs, and other constituencies. The majority of VAERS reports are received from vaccine manufacturers and health care professionals. More information about VAERS can be found at <https://vaers.hhs.gov/>.

Phonetic and Orthographic Computer Analysis (POCA)

POCA is a system designed by FDA and is publicly available by requesting the system from FDA.⁴⁹ POCA is an analytical tool designed to help identify drug and biologic names that are phonetically and orthographically similar to one another. The Alignment of Phonetic Sequences (ALINE) algorithm is used to calculate the phonetic score. The orthographic component of the current algorithm was revised in December 2016 to accommodate the changing trends in medication errors due to technological changes. The revised new algorithm is designed to better capture the shift in the type of errors that are being reported due to using electronic prescribing. The algorithm has been revised to put more emphasis on similarity that occurs at the beginning of the word, especially the first three letters (bigram or trigram), and on exact letter matches. The algorithm continues to have emphasis on consecutive exact matches but also emphasizes where names share letters that are not consecutive. Several new score metrics (i.e., sub-algorithms) are combined in various ways to formulate the final score.⁵⁰

⁴⁹ Available at <https://www.fda.gov/drugs/information-industry-drugs/phonetic-and-orthographic-computer-analysis-poca-program>.

⁵⁰ *Modified Adaptive Algorithm*: Modified the existing bi-gram matching algorithm to account for reverse confuse lookups. *Initial Match*: Check up to first n matching letters. This is to accommodate beginning letter(s) overlap.

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166 POCA search provides three data sets: (1) combined orthographic and phonetic matches, (2)
167 phonetic matches, and (3) orthographic matches. The threshold FDA uses to conduct the
168 orthographic and phonetic searches is set at a combined score of 55%, based on the validation
169 work done on the POCA algorithms.

170 171 ***Drugs@FDA***

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173 Drugs@FDA, is an FDA website that contains most of the drug and therapeutic biological
174 products approved in the United States since 1939. The majority of labeling, approval letters,
175 reviews, and other information are available for products approved from 1998 to the present.
176 Drugs@FDA contains information about FDA-approved *brand name* and *generic drugs*;
177 *therapeutic biological products*, *prescription* and *over-the-counter* human drugs; and
178 *discontinued drugs*. See Drugs@FDA, available at
179 <https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm>.

180 181 ***RxNorm***

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183 RxNorm is publicly available and contains the names of prescription and many OTC drugs
184 available in the United States. RxNorm includes generic and branded drug products and
185 packaging configurations. Radiopharmaceuticals, contrast media, food, dietary supplements, and
186 medical devices, such as bandages and crutches, are not included in RxNorm (see RxNorm,
187 available at <http://www.nlm.nih.gov/research/umls/rxnorm/overview.html#>).

188 189 ***USAN Stems***

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191 The USAN Council (tri-sponsored by the American Medical Association (AMA), the United
192 States Pharmacopeial Convention, and the American Pharmacists Association) aims for global
193 standardization and unification of drug nomenclature and related rules to ensure that drug
194 information is communicated accurately and unambiguously. The USAN Council works closely
195 with the International Nonproprietary Name Programme of the World Health Organization, and
196 various national nomenclature groups. The website is publicly available, managed by the AMA,
197 and contains lists of all the recognized USAN stems (available at [https://www.ama-](https://www.ama-assn.org/about/united-states-adopted-names/united-states-adopted-names-approved-stems)
198 [assn.org/about/united-states-adopted-names/united-states-adopted-names-approved-stems](https://www.ama-assn.org/about/united-states-adopted-names/united-states-adopted-names-approved-stems)).

199 200 ***Medical Abbreviations References***

201
202 Various references on this topic are available. These references contain commonly used medical
203 abbreviations and their definitions.

Longest Common Subsequence: the longest group of letters from two words that are common between the two groups and in the same order in each group. *Unigram Match*: This metric gives priority to overlapping letters fixed in the same position. *Longest Common Substring*: This metric gives priority to drug names embedded within another drug name.

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Appendix A: Examples of Previously Used Modifiers and Their Commonly Understood Meanings

Modifiers	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 oral contraceptive
Fe	Used to indicate ferrous component

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Appendix B: Research Methodology for Conducting Misbranding Review

For sponsors that wish to submit data on a proposed proprietary name, FDA recommends an experimental method as part of the approach to determine whether a proposed proprietary name is misleading because this method enables interpretation of causal relationships between variables. That is, by controlling all other experimental factors besides the drug name, researchers can be confident that the name itself caused particular responses. Box 1 provides one possible approach for such an evaluation. Other approaches may be appropriate. The approach described in Box 1 should be especially helpful in gathering information about how a name influences attitudes and behaviors of a practicing health care professional. If participants are only asked what they think about the proposed name, it will be difficult to determine how accurately their responses reflect their actual thoughts or likely behaviors, because participants may state what they think they should state, or what they think the investigators want to hear. Comparing the responses to the proposed name with responses to the neutral control name, however, could determine whether the proposed name influences these thoughts and intended behaviors.

a. Design of Questions

A combination of open-ended and closed-ended questions, arranged from more general to more specific, should be used. Questions should be designed to avoid leading questions, yea-saying and other forms of bias.¹ Initial questions in the study should be asked before participants have any information about the product so that the answers will not be influenced by knowledge of product characteristics. Subsequent questions would be asked after receiving indication information for the product but no other identifying information. Because investigational new drug (IND) studies form the basis of ultimate determinations about the efficacy and risk of a drug product seeking approval, specifics may not be known at the time the proprietary name is proposed and undergoing testing. Therefore, there should be a measure of participant response when participants have only minimal information.

Box 1: Possible Evaluation Design

¹ For a brief discussion of questionnaire bias in label comprehension studies, see Morris, L.A., Lechter, K., Weintraub, M., et al., Comprehension testing for OTC drug labels: Goals, methods, target population, and testing environment. *Journal of Public Policy and Marketing*. 1998;17(1):86-96.

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The FDA recommends as one possible approach a crossover design in which the proposed proprietary name is evaluated in the context of both a neutral control name and an extreme control name. This involves splitting the study participants into two groups, both of whom will evaluate the proposed proprietary name but in a different order from each other.

Before testing the proposed proprietary name, two control names should be established through pretesting:

- A neutral control name that is pretested to ensure that it makes no representations at all (i.e., it is neutral from a promotional standpoint) should be established.
- An extreme control name that is pretested to ensure it makes clear misrepresentations should be established.

All the participants will respond first to questions about the neutral control name, described above. Next, half of the participants respond to the proposed name and then to the extreme control name described above. The other half of the participants respond to the extreme control name first and then to the proposed name.

The study questions used as outcome measures should cover perceptions elicited by the proposed name that are of a promotional nature (e.g., product safety, efficacy, indication, superiority), as well as questions designed to elicit aspects of behavioral intent (e.g., likelihood to prescribe). A comparison of interest is participant responses to the proposed name compared with responses to the neutral control name. The extreme name serves as a positive control to ensure that individuals can identify names that make representations about efficacy, safety, or other promotional aspects.

The FDA suggests that the neutral and extreme names be fictitious in nature to control for participants' prior experience and attitudes. Existing names could be acceptable as neutral or extreme controls if they are pretested and shown to possess the desired experimental qualities outlined above.

Sponsors may choose to select different neutral and extreme control names for each study, or they may choose to use the same neutral and extreme control names for multiple studies. Participants should be exposed to the neutral control name only once across studies; that is, sponsors that choose to use the same neutral name in more than one study should choose a new set of participants for that study to ensure that participants have not previously responded to the neutral name.

Examples of questions include:

- You have just learned of a new product named DRUG X. What, if anything, does the name DRUG X say or suggest to you about the product? (*open-ended question*)

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- 296 • Based on this name, which of these conditions do you think DRUG X treats? (please
297 choose the best answer) (*closed-ended question*)
- 298 - Condition 1
299 - Condition 2
300 - Condition 3
301 - Condition 4
- 302 • Based on this name, how effective or ineffective would you say DRUG X is?
303 - Very effective
304 - Somewhat effective
305 - Somewhat ineffective
306 - Very ineffective
- 307 • Based on this name, how safe or unsafe would you say DRUG X is?
308 - Very safe
309 - Somewhat safe
310 - Somewhat unsafe
311 - Very unsafe
- 312 • Now you learn that product DRUG X is used to treat CONDITION Y. What does this
313 name mean to you in this context?
- 314 Based on this name, how safe or unsafe would you say it is to use DRUG X to treat
315 CONDITION Y?
- 316 - Very safe
317 - Somewhat safe
318 - Somewhat unsafe
319 - Very unsafe
- 320 Based on this name, how effective or ineffective would you say DRUG X is to treat
321 CONDITION Y?
- 322 - Very effective
323 - Somewhat effective
324 - Somewhat ineffective
325 - Very ineffective
- 326 • If DRUG X were available, how likely would you be to prescribe DRUG X for
327 CONDITION Y?
- 328 - Not at all likely
329 - Somewhat likely
330 - Moderately likely
331 - Very likely
- 332 • On a scale from 1 to 5, where 1 equals *Strongly Disagree* and 5 equals *Strongly Agree*,
333 please indicate your agreement or disagreement with the following statement:
334 *This name suggests superiority over other products with the same indication.*
335

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336 **b. Sampling**

337

338 These are general comments. A statistician should be consulted before making definitive
339 determinations about sample size and sampling design. The size of the study participant sample
340 should be adequate to detect differences. The sample should represent the relevant prescribing
341 population and be generalizable to this population. In addition, sponsors should consider testing
342 a sample of consumers. Although this group does not have prescribing authority, consumers
343 should and do participate actively in treatment decisions. The product name may play a role here
344 through direct-to-consumer advertising.

345

346 **c. Submission to FDA**

347

348 If submitting data on a proposed proprietary name, sponsors should submit to the appropriate
349 center for evaluation of all research methodology used to support that proposed proprietary
350 name. This includes a description of participant demographics; the study methodology
351 (protocol); the product profile provided to study participants; the complete study questionnaire,
352 including any screening questions; the coding scheme used to analyze open-ended questions;
353 complete study results (both positive and negative), including results of pretests; and any other
354 information given to the study participants regarding the drug approval process (e.g., copies of
355 FDA regulations given to study participants).

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Appendix C: Research Methodology Considerations for Conducting Name Simulation Studies

Generally, name simulation studies test how subjects respond to a proposed proprietary name by asking them to use the name in use conditions that simulate the real world. The more closely and fully the simulation approximates real-world use conditions, the more generalizable the results of the simulation testing. Name simulation tasks should reflect the full range and variety of tasks involved in the prescribing, transcribing, dispensing, and administering of drugs. Simulations should include common 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 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. For example, when considering a product that is dosed on milligram/kilogram basis, consider using an average weight-based dose for the intended population in the simulation study.

a. 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).² FDA recognizes that a study of this magnitude is not realistic. However, a well-designed parallel group observational study consisting of the 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 the potential prescribing conditions for the proposed product. We recommend that actively practicing health care professionals, such as prescribers, medical transcribers, pharmacists, pharmacy technicians, or nurses, who administer the products in the proposed use conditions for the product be included in the study.

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). For a name that was misinterpreted, data should include whether the name was misinterpreted as another drug name or whether there were trends in spelling misinterpretations for specific letters.

² This calculation was made to determine whether the error rate differs from 0.001 at a 0.05 significance level and 80% power, assuming the medication error rate of the sample is 0.0005.

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401 **b. Participants**

402
403 All participants in name simulation studies should be actively practicing health care
404 professionals, such as prescribers, medical transcribers, pharmacists, pharmacy technicians, or
405 nurses, who administer the products in the proposed use conditions for the product. Sponsors
406 should take care to ensure that participants are representative of the full range of persons
407 involved in a given scenario. The study should simulate the full range of settings where the
408 product could be used, such as community pharmacy, ambulatory care, hospital, or long-term
409 care. For example, if the product will be dispensed in an inpatient setting, the participants should
410 include, but not be limited to, inpatient pharmacists, pharmacy technicians, ward clerks, and
411 nurses. When evaluating proprietary names for specialty drugs, sponsors should consider
412 whether the specialty drug could be at risk for entering into broader health care contexts. If so,
413 sponsors should consider including primary care practitioners, pharmacists, pharmacy
414 technicians, and nurses to probe which product names outside the specialty might cause error.
415 These stakeholders will bring experience from different workflow and practice environments.

417 **c. Number of Scenarios**

418
419 For an adequate descriptive assessment, sponsors should test an adequate number of scenarios to
420 provide a concomitant benefit in accuracy and reliability of the study outcomes. Scenarios may
421 vary depending on the type of setting and should be appropriate for the product being tested.
422 Participants involved in a name simulation study can participate in the testing of multiple
423 proposed proprietary names. However, to minimize bias, a name should be tested only once by
424 the same participant in the written and spoken scenarios.

425
426 Each anticipated prescribing condition for the proposed product should be tested several times,
427 considering all relevant modes of communication (such as spoken, written, computer order entry,
428 computer selection, and selection of product from drop-down menu). For example, for a product
429 that is administered only intravenously in an inpatient setting, an outpatient simulation using a
430 handwritten prescription might not be helpful. A simulation for an orally administered product
431 that could be dispensed in either inpatient or outpatient settings should contain all possible
432 inpatient and outpatient scenarios. When appropriate, these scenarios should be revised to
433 reflect, as closely as possible, the likely health care setting(s) for using the product, including
434 how the product will be prescribed, how the prescription will be transcribed, and how the
435 product will be dispensed and administered.

436
437 Sponsors should consider embedding the test name in a list of two or three other proprietary
438 names of marketed products in the simulated prescriptions, or consider using other simulated
439 prescription formats that are designed to mimic actual use. Spoken orders should include several
440 scenarios with an unaided pronunciation and several scenarios with a pronunciation based on
441 how the sponsor proposes to pronounce the name when marketed (for example, *Kaletra* is
442 pronounced by some as Kuh-let-ra and the sponsor's pronunciation is Kuh-lee-tra).

443
444 At the end of a simulation, each participant should be interviewed, preferably using nonleading
445 scripted follow-up questions. The participant responses should be recorded verbatim. All
446 qualitative data derived from follow-up questioning should be coded and analyzed. The

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447 verbatim responses might confirm or further describe a potential for confusion. More
448 importantly, responses might identify additional names of concern that were not identified
449 through a manual database or computational searches. The names identified from the simulation
450 study should then be evaluated as outlined in section IV of this guidance to assess the likelihood
451 of confusion with the proposed name.

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Appendix D: Highly Similar Name Pair Checklist

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

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.			
<u>Orthographic Checklist</u>		<u>Phonetic Checklist</u>	
Y/N	Do the names begin with different first letters? <i>Note that even when names begin with different first letters, certain letters may be confused with each other when scripted.</i>	Y/N	Do the names have different number of syllables?
Y/N	Are the lengths of the names dissimilar when scripted or printed? <i>FDA considers the length of names different if the names differ by two or more letters. This may be dependent on the position of the letters within the name and which letters are used. Some letters are more noticeable than others (e.g., "m" is a wide, noticeable letter).</i>	Y/N	Do the names have different syllabic stresses?
Y/N	Considering variations in scripting of some letters (such as <i>z</i> and <i>f</i>), 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?		

Appendix E: Moderately Similar Name Pair Checklist

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Moderately Similar Name Pair Checklist (i.e., combined score is $\geq 55\%$ to $\leq 69\%$)

Step 1	<p>Review the DOSAGE AND ADMINISTRATION and HOW SUPPLIED/STORAGE AND HANDLING sections of the Prescribing Information to determine whether 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.</p> <p>For single-strength products, also consider circumstances where the strength may be omitted.</p> <p>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.</p> <p>To determine whether the strengths or doses are similar to your proposed product, consider the following list of factors that may increase confusion:</p> <ul style="list-style-type: none">○ Alternative expressions of dose: for example, 5 milliliters (mL) may be listed in the Prescribing Information, but the prescription may express the dose in metric units (e.g., 500 milligrams (mg)) or in non-metric units (e.g., 1 teaspoon, 1 tablet/capsule). Similarly, a strength or dose of 1,000 mg may be expressed, in practice, as 1 gram, or vice versa.○ Presence of trailing zeros or absence of leading zeros: for example, 10 mg (if written as 10.0 mg) is similar in appearance to 100 mg, which may potentiate confusion between a name pair with moderate similarity. Additionally, 0.1 mg can be confused with 1 mg if written without a leading zero (.1 mg).○ Similar sounding doses: for example, 15 mg is similar in sound to 50 mg.
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Step 2	<p>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 <u>with</u> overlapping or similar strengths or doses.</p>	
	<p style="text-align: center;"><u>Orthographic Checklist</u> (Y/N to each question)</p> <ul style="list-style-type: none"> • 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 <i>z</i> and <i>f</i>), 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? 	<p style="text-align: center;"><u>Phonetic Checklist</u> (Y/N to each question)</p> <ul style="list-style-type: none"> • 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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Appendix F: Low Similarity Name Pairs

Low Similarity Name Pairs (i.e., combined score is $\leq 54\%$)

- Names with low similarity are generally acceptable 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 evaluate the name pair as moderate similarity and review according to the moderately similar name pair checklist (see Appendix E).

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