PDUFA PILOT PROJECT

PROPRIETARY NAME REVIEW

DRAFT CONCEPT PAPER

(For Discussion at June 5 and 6, 2008, Meeting)

May 2008

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I. INTRODUCTION

On September 27, 2007, President Bush signed into law the Food and Drug Administration Amendments Act of 2007, Pub. L. 110-85, 121 Stat. 823 (FDAAA), which includes the reauthorization and expansion of the Prescription Drug User Fee Act (PDUFA IV). The reauthorization of PDUFA significantly broadens and upgrades the Food and Drug Administration's (FDA) drug safety program and facilitates more efficient development of safe and effective new medications for the American public. As part of the reauthorization of PDUFA IV, FDA committed to certain performance goals in its goals letter.[1] As one of these goals, FDA stated that it would use user fees to implement various measures to reduce medication errors related to look-alike and sound-alike proprietary names and to such factors as unclear label abbreviations, acronyms, dose designations, and error-prone label and packaging design.

In addition, FDA agreed to develop and implement a pilot program to enable pharmaceutical firms participating in the pilot to evaluate proposed proprietary names and to submit the data generated from those evaluations to the FDA for review.[2] In accordance with these goals, FDA is developing and implementing a pilot program that will enable participating pharmaceutical firms to evaluate their proposed proprietary names and submit the data generated from those evaluations to the FDA for review.

Using *best practices* when carrying out their own proprietary name reviews and providing FDA with the data that result from those reviews may help ensure that pharmaceutical firms choose appropriate proprietary names for their products and avoid names that are misleading or that are likely to lead to medication errors, making FDA's application review more efficient. At the end of the pilot, FDA will evaluate the results to determine whether the model of industry conducting reviews, submitting the results to FDA, and FDA reviewing the data would be a better model than FDA conducting de novo reviews of proprietary names.

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[1] See goals letter from the Secretary of Health and Human Services to the Chairman of the Committee on Health, Education, Labor, and Pensions of the Senate and the Chairman of the Committee on Energy and Commerce of the House of Representatives, as set forth in the Congressional Record, at http://www.fda.gov/oc/pdufa4/pdufa4goals.html.

[2] For more on FDAAA, PDUFA 4, and the goals letter, *see* http://www.fda.gov/oc/pdufa/default.htm.

The Centers[3] have identified the following goals as part of the process of fulfilling the provisions of the goals letter:

1. Hold a public technical meeting (currently scheduled for June 5 and 6, 2008) to discuss the planned pilot program and the reviews that will be completed as part of the pilot program
2. Make available by the end of FY 2008 a concept paper describing the pilot and the proprietary submissions that will be made as part of the pilot
3. Begin enrollment into the pilot program by the end of FY 2009.
4. Evaluate the pilot program by the end of FY 2011 (or subsequent to accruing two years of experience with pilot program submissions) to determine whether it is feasible and efficient to have applicants perform their own name analysis and submit resulting data to FDA

This draft concept paper is being made available for discussion at the June 2008 meeting. Comments on the concept paper can be brought to the meeting, or submitted to the Docket (number FDA-2008-N-0281). The Docket will remain open for a period of time following the June meeting to enable interested parties to submit comments.

II. BACKGROUND

During the past two decades, FDA has considered the role of names and naming processes in medication errors as part of the Agency's focus on the safe use of medical products. FDA has developed internal procedures and processes that are part of its marketing application review process for evaluating the potential for a proposed product name (submitted as part of a new drug application (NDA), biologic license application (BLA), or abbreviated new drug application (ANDA) to cause or contribute to medication errors. The goal of the pilot program is to test a process that, ultimately, could enable pharmaceutical manufacturers to carry out proprietary name reviews of their products prior to submitting marketing applications to FDA, so that the FDA review of proprietary names would be more efficient.

The following discussion reviews briefly how naming can contribute to medication errors and what recent activities have lead to current efforts to involve product sponsors in the drug name review process.

A. Medication Errors

The Centers use the definition of a *medication error* as set forth by the National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP). Specifically, a

[3] For purposes of this document, the Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER) will be referred to as the "Centers."

medication error is "any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the healthcare professional, patient, or consumer."[4] It is important to note that medication errors are considered to be preventable events and that the risk of errors can be detected in the premarket stage of product development using simple test methods.

Medication use errors occur due to sound-alike or look-alike names, unclear labels, or poorly designed packaging.[5] In the U.S. medication-use system, healthcare providers rely on a product's name as the critical identifier of the appropriate therapy in a market of thousands of products. Therefore, accurate interpretation of a product's name is essential to ensure that the correct product is procured, prescribed, prepared, dispensed, and administered to the patient. Product names that look or sound alike can lead to medication errors and potentially to patient harm by increasing the risk of a healthcare provider's misprescribing or misinterpreting the correct product name, dispensing and/or administering the wrong product, or dispensing it incorrectly.

Because product name confusion can occur at any point in the medication use process, the Centers consider the potential for confusion throughout the entire U.S. medication use process, including product procurement, prescribing/ordering, dispensing, administration, and monitoring the impact of the medication.[6]

Medication use within a healthcare organization can be viewed as a system, with several components and processes: inputs (patient and drug therapy information), throughputs (care provided), and outputs (effective, efficient, and safe treatment).[7] Depending on the setting and organization, there are many variables potentially interacting within this system. Such variables may include, but are not limited to:

- Different processes and procedures
- Different types of healthcare providers involved
- Different patients
- Different products
- Different storage and dispensing conditions
- Different available technologies

Because of the many potential interactions among the system elements, multiple opportunities for medical care-related confusion and medication errors exist.

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4 National Coordinating Council for Medication Error Reporting and Prevention (Definition of Medication Error) at http://www.nccmerp.org/aboutMedErrors.html.

5 Institute of Medicine, *To Err is Human – Building a Safer Health System (*1999).

6 Institute of Medicine, *Preventing Medication Errors*.

7 Joint Commission on Accreditation of Healthcare Organizations, *Medication Use: A Systems Approach to Reducing Errors.*

This concept paper explains the Centers' current thinking about how NDA or BLA applicants would be able to assess a proposed proprietary name for safety (i.e., potential for medication errors) and/or promotional aspects prior to NDA or BLA approval and subsequent marketing in the United States and submit the results of the assessment for review under the planned program provided for in the goals letter. This concept paper is intended to facilitate public discussion about these topics and encourage public comment on the recommendations proposed herein.

As described more fully in the next section, the evaluation of proprietary names has been discussed numerous times in the past, most recently at two public meetings in 2003 among the Centers, industry, and other stakeholders. A third public meeting, which is scheduled for June 5 and 6, 2008, will focus on any subsequent developments in the science and practice of proprietary name analysis since the 2003 meetings, the strength of evidence for current approaches to name review as discussed in this paper, the elements of *best practices* in testing in the absence of a *gold standard*, and on details of how the planned pilot program should be structured and evaluated.

B. 2003 FDA Public Meetings on Drug Naming

In June 2003, the Centers, together with the Institute for Safe Medication Practices (ISMP) and the Pharmaceutical Research and Manufacturers of America (PhRMA), held a public meeting to discuss the proper approach to proprietary name evaluation. This meeting was the first public discussion of current methods to screen potential proprietary drug names for similarities to names of currently marketed drugs. Much of the information on the Centers' name evaluation process presented at the meeting is available on the FDA Web site.[8] Specific topics discussed at the June 2003 meeting included:

- The size, qualifications, and best use of internal expert teams to evaluate proprietary names
- Challenges in designing questionnaires for the assessment of proprietary names
- The methodology for conducting a Failure Mode and Effects Analysis (FMEA)
- Handwritten prescription and medication requisition recognition techniques
- Use of computational linguistic methods and string matching to identify sound-alike or look-alike proprietary names
- Sampling frames and methods to identify name evaluation study participants
- Use of computer-assisted decision analysis tools

At the June 2003 public meeting, many meeting participants offered these views:

- Prescription and order simulations should reflect actual situations as much as possible.

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[8] *See* http://www.fda.gov/cder/ meeting/drugNaming.htm.

- Simulations should replicate medication order situations with known error vulnerabilities.
- The risk of a medication error can be increased or reduced, depending upon how medication orders are communicated (e.g., oral, written, physician order entry, or electronic prescribing).
- Simulations should include not only the product name, but also the strength, quantity to dispense, directions for use, and patient age and weight (for pediatric patients).
- Nonprescription (over-the-counter or OTC) drug products should also be subject to the same proprietary name testing standards as prescription drug products.

More global issues were also discussed at the meeting. Specifically, stakeholders in the drug application process indicated that they consider the current proprietary name testing approach to be only qualitative in nature. The processes and outcomes of the Centers' trade name review were perceived as inconsistent across reviews and FDA approval units and most of the current approaches to proprietary name reviews could not be validated or reproduced. Because of these issues, the stakeholders and FDA expressed the opinion that there is no *gold standard* for testing proprietary drug product names to assess the risk of error. However, all of the methods discussed were considered to offer value in the name testing process and, in the absence of a *gold standard*, participants stated that multiple tests should be conducted complementarily with a systematic approach, and standardized tools should be applied.

C. December 2003 Meeting

In December 2003, FDA held a meeting of its Drug Safety and Risk Management Advisory Committee (DSARM). At that meeting, the June 2003 public meeting results were reviewed, additional topics in proprietary name evaluation testing were presented, and public comments were elicited. Materials from the December 2003 meeting are available on the FDA Web site.[9]

At the December meeting, the DSARM concluded that, although the current name testing approaches appeared logical and were under refinement, a scientifically valid, outcomes-based, data-driven approach to analyzing proprietary drug product names still did not exist.

D. June 5 and 6, 2008, Meeting

A third public meeting, scheduled for June 5 and 6, 2008, will focus on any subsequent developments in the science and practice of proprietary name analysis since the 2003 meetings, the strength of evidence for the current approaches to name review as discussed in this concept paper for both prescription and nonprescription products, the elements of *best practice* in testing in the absence of a *gold standard*, and on details of how the planned pilot program should be structured and evaluated.

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[9] *See* http://www.fda.gov/ohrms/dockets/ac/03/slides/4007s1.htm.

This concept paper is intended to facilitate discussion of the proposed pilot program at the June meeting. To focus discussion, the concept paper contains:

(1) A summary of plans and logistics to date on the proposed pilot program

(2) Recommendations, based on FDA's current review processes, on how applicants can assess a proposed proprietary name for safety (i.e., potential for medication errors) as part of the pilot program

(3) A discussion of how the Agency will evaluate the pilot project submissions

Some general information on data sources is provided in the Appendix.

FDA is seeking public input at and after the June 5 to 6 meeting on the elements of a proprietary name analysis, including the development of a pilot program for applicants to assess potential proprietary names; the Centers' evaluation of these name analyses; and this pilot program. Comments can be submitted to Docket number FDA-2008-N-0281, which was established with the announcement of the June 2008 meeting notice. The comment period will be extended for a period of time following the June meeting to enable interested parties to submit their comments.

III. PDUFA PILOT PROGRAM—LOGISTICS

As outlined above, one of the Centers' performance goals under PDUFA IV is to develop and implement a pilot program that would enable participating pharmaceutical firms to evaluate proposed proprietary names and submit the data generated from those evaluations to the Centers for review. Using *best practices* when carrying out their own proprietary name reviews and providing FDA with the resulting data may help ensure that pharmaceutical firms are able to choose appropriate proprietary names for their products (e.g., not misleading or likely to lead to medication errors), thus making FDA's application review more efficient.

FDA proposes the following general plans for the pilot project, but as indicated, is interested in input from potential participants.

A. What Are the General Logistics of the Pilot Program?

The Centers expect that enrollment in the pilot program for proprietary name analysis will begin by the end of FY 2009 (September 30, 2009). Applicants will be asked to pre-register.[10] Participation in the pilot program is voluntary for applicants, though the Centers expect that many applicants will be interested in participating. The Centers hope that during the two-year enrollment period they will be able to receive and review approximately 25 to 50 proposed proprietary name submissions under the pilot program. To achieve this goal, the Centers plan to

[10] Registration procedures are still being developed.

accept on average one or two submissions per month. The Centers expect that enrollment will last for two years. At the end of the two-year period, the Centers will evaluate the pilot program.

B. How Will the Pilot Program Function?

The Centers propose that proprietary name analyses under the pilot program be submitted to the Centers either during the investigational new drug application (IND) process, or as part of the initial submission of the NDA, BLA, or ANDA. The Centers propose that submissions during the IND phase be accepted ***only*** for products that have completed phase 2 of clinical development.

Applicants should notify the Centers as soon as possible once they have determined that they would like to submit a specific proprietary name evaluation under the pilot program. We recommend that applicants contact the appropriate center 120 days prior to the anticipated date of a proposed proprietary name submission to discuss the planned submission.

The Centers will answer questions submitted in writing; in rare circumstances, a face-to-face meeting to discuss the planned submission may be appropriate.

C. What If I want to Deviate from the Process in the Concept Paper?

If applicants plan to deviate from the proposed proprietary name evaluation process outlined in the formally issued concept paper (after the June meeting), they should inform the Centers at the 120-day discussion. However, the Centers do not have the resources and therefore do not intend to review proposed alternative methodologies with the intent of coming to agreement with an applicant on the acceptability of these alternative methodologies. In such cases, the Centers' review of the alternative methodologies will occur during the review of the actual submission.

D. Why Do I Have to Make Two Submissions?

For purposes of the pilot program, applicants will be asked to submit two separate sets of drug name-related information. The first set should include the information applicants submit under the Agency's current practice. The other submission should include the applicant's comprehensive evaluation of the proposed proprietary name as described in Section IV of this paper (a recommended template has been provided in Attachment B). The Centers will be able to perform two separate, independent reviews and compare the results as described below.

The first review will evaluate an applicant's proprietary name evaluation using the data submitted by the applicant obtained from the test methods outlined in this paper. The second review will independently analyze the proposed proprietary name using the Centers' traditional approach to review of proposed proprietary names. The two reviews will be conducted by two different reviewers, who will not share with each other any details of the data or other findings during the review process. At the end of the review process (i.e., when each reviewer has come to a conclusion regarding the acceptability of the proposed proprietary name), the two reviewers, along with Centers' other experts in proprietary name review, will meet to discuss the data and their conclusions. At that time, the two reviewers will note any differences in the data, findings,

and conclusions between the two analyses and reviews. Discussion will focus both on the differences in the outcomes of specific analyses, as well as on differences in the overall conclusion regarding the acceptability of the proposed proprietary name.

E. What If My First Choice Name is Not Acceptable?

Under the pilot program, the Centers will continue their long-standing practice of reviewing the first-choice name. If the Centers determine that the first-choice name is acceptable, the Center will not review the second-choice name. If the Centers determine that the first-choice name is not acceptable, the review clock will be stopped. At that time, the Centers will notify the applicant, in writing, of their decision regarding lack of acceptability of the proposed first-choice name. The review clock will not re-start until the applicant either has informed the Centers, in writing, that it would like its originally submitted second-choice name reviewed, or when FDA receives an applicant's submission of an alternative second-choice name along with the comprehensive information described below in section III F. At that time, the Centers will begin review of the second-choice name. In the latter scenario, if an applicant has submitted a complete proprietary name analysis for the second-choice name, the responsible Center will use discretion to determine whether to review the applicant's analysis or conduct its own analysis. Although the Centers would ideally review the applicant's completed proprietary name analysis for the second-choice name, factors such as staffing and timelines will be used in making this determination.

F. What Happens To My Submission and How Will It Be Reviewed?

Once the Centers receive a proprietary name submission under the pilot program, they will determine if the submission contains the comprehensive information essential for evaluation of the proposed name. A comprehensive submission is one that contains:

- At least one proposed proprietary name
- Identification of the first-choice proprietary name, if more than one name is submitted
- Data-driven analyses of the acceptability of the proposed proprietary name, including a clear description of the methods, the data sources, and the data
- Data needed to evaluate the proprietary name under the traditional review process

The Centers will encourage applicants to submit proprietary name evaluations based on the methods set forth in the concept paper. However, an applicant's completion and submission of these evaluations is not necessary for the Centers to consider a submission complete. Applicants can submit alternative evaluations. If, on their face, these evaluations are data-driven, the Centers will accept the submissions.

If the Centers determine that a submission of a proprietary name evaluation is incomplete, it will inform the applicant promptly.

G. What Will the Agency Review in Determining a Proposed Name's Acceptability?

Once the Centers determine that a submission of a proprietary name evaluation contains the comprehensive information essential for substantive review, they will undertake parallel reviews. The Centers' regulatory decision on the acceptability of a proposed proprietary name under the pilot program will be based on review of data from the applicant's analysis and from the Centers' independent analysis. In addition, the Centers will use the data to evaluate the overall pilot program.

H. Will IND and NDA/BLA Submissions Be Handled Differently?

When the Centers receive a submission of a proposed proprietary name evaluation under the pilot program during the IND phase, it will aim to complete its two independent reviews and arrive at a decision within the timelines stipulated under PDUFA IV (180 days from receipt of complete submission in 50 percent of cases in FY 2009 and 180 days in 70 percent of cases in FY 2010). When the Centers receive a submission of a proposed proprietary name evaluation under the pilot program at the time an NDA or BLA is submitted, they will aim to complete their two independent reviews and arrive at a regulatory decision within the timelines stipulated in PDUFA IV (90 days in 50 percent of cases in FY 2009 and 90 days in 70 percent of cases in FY 2010). Proprietary names submitted as part of an ANDA are not subject to the timelines stipulated in PDUFA IV, but will be reviewed with a goal of 180 days.

I. When and How Will the Pilot Program Be Assessed?

At the end of FY 2011, or subsequent to accruing two years of experience with pilot program submissions, the Centers will evaluate the pilot program. The Centers anticipate that evaluation of the program will focus primarily on a comparison of the conclusions the Centers have reached after review of applicants' analyses of proposed proprietary names to those the Centers reach after their own analyses. In addition, the Centers intend to examine patterns, if any, of differences between their own analyses and those performed by applicants and between their interpretation of the results of specific applicant analyses, applicants' interpretations of the same results, and the ultimate regulatory decision that was made based. The Centers expect that these evaluations will be largely qualitative. Any quantitative evaluations will be descriptive. The results of this pilot program will be discussed in a public meeting in FY 2013 or before.

IV. ASSESSING PROPOSED PROPRIETARY NAMES IN PILOT PROGRAM

In the following sections, proposals and recommendations about how to assess proprietary names reflect the Agency's thinking and processes as currently practiced. The goals in Section IV are two fold: (1) explain and clarify what the Agency's current assessment involves and (2) recommend approaches pharmaceutical manufacturers should use when performing their assessments under the pilot program.

The Center's primary consideration when evaluating the acceptability of a proposed proprietary name is avoiding the potential for medication errors. The Centers believe that no single test is sufficient to reach a conclusion that a proprietary name is acceptable. The Centers emphasize

that the best approach has proved to be using a combination of tests to evaluate name appropriateness.

FDA review of proprietary names includes consideration of both safety and promotional aspects. The safety review of a proposed name is based on the findings of a Failure Modes and Effects Analysis (FMEA) of the proprietary name and is focused on the avoidance of medication errors. FDA not only considers the potential for a name to be spelled similarly and/or sound similar to a currently marketed product or one that is in the approval pipeline, but also considers the potential for the proposed name to inadvertently function as a source of error for reasons other than look- and sound-alike name confusion, for instance whether the abbreviation for a drug product would be similar to the abbreviation of another drug product.

The promotional review of proposed names also considers whether the name functions to overstate the efficacy, minimize the risk, broaden the indication, make unsubstantiated superiority claims for the product, or is overly "fanciful" (21 CFR 201.10(c)(3)). Consideration also is given to the proposed product's characteristics, including its intended use, dosage form and strength, and route of administration because the product characteristics provide a context for communication of the product name and ultimately determine the use of the product in the usual clinical practice setting. The following sections provide a more detailed snapshot of the Agency's proprietary name review.

There is concern that the same methods described for prescription products should not be employed in the assessment of a nonprescription product name because those products are most often purchased by patients or consumers with or without the oversight of a healthcare provider. We are seeking input on whether the proposed approaches for minimizing medication errors for nonprescription products should consider solely the input from consumers, should follow the methods described for prescription products, or whether an alternative approach should be used.

A. Safety Review

The Centers' safety review of a proprietary name involves methods that generate a list of names that could be confused with the proposed proprietary name as well as methods to test the likelihood of confusion between these names and the proposed proprietary names.

1. Preliminary Screening

Names often fail the Centers' screening process for readily identifiable reasons. The common practices in Box 1 (next page) reflect known causes of, or contributors to, medication errors. If a proposed name fails the preliminary screening, it is unlikely to be a viable candidate for a proprietary name. The Centers recommend that applicants consider the common errors listed in Box 1 to perform a preliminary screening of their proprietary name for acceptability prior to testing.

2. USAN Stem Search

In their review of drug names, the Centers screen proposed proprietary names against the stem list created by the United States Adopted Names (USAN) Council. The purpose of the Counsel is to serve the health professions in the United States by selecting simple, informative, and unique nonproprietary names for drugs products Selections are made by establishing logical nomenclature classifications based on pharmacological and/or chemical relationships.

The USAN Council (tri-sponsored by the American Medical Association (AMA), the United States Pharmacopeial Convention (USP), and the American Pharmacists Association (APhA)) works closely with the International Nonproprietary Name (INN) Programme of the World Health Organization (WHO) and various national nomenclature groups to achieve global standardization and unification of drug nomenclature and related rules with the goal of ensuring that drug information is communicated accurately and unambiguously.

The Centers propose that applicants identify names that are not viable candidates by screening against the USAN stem list. The Centers also propose that all proprietary name submissions include a statement indicating that the name does not contain a USAN stem and the date on which this information was searched on the USAN list.

Box 1: Common Practices Known for Causing and Contributing to Medication Errors

Dosing Interval
The Centers discourage proprietary names that incorporate or suggest a dosing interval (e.g., NameBID). Drug product characteristics and/or drug release characteristics are subject to change over time with approval of new dosing intervals, thus possibly rendering the original proprietary name misleading.

Dosage Form/Routes of Administration
The Centers discourage the use of proprietary names that incorporate or suggest a particular dosage form (e.g., Nametabs, Namecaps) or route of administration (*e.g.*, Nameoral). Avoiding the suggestion of a dosage form or route of administration in the name will enable a company to use the same proprietary name for future dosage forms of the product without making the proprietary name misleading.

Medical And/Or Product Name Abbreviations
The use of common medical abbreviations and coined abbreviations in a proprietary name may be misinterpreted and therefore should generally be avoided. Abbreviations commonly used for prescription communication, especially abbreviations recognized as error-prone and potentially dangerous by the Institute for Safe Medication Practices (www.ISMP.org/tools/errorproneabbreviations.pdf) and the National Coordinating Council on Medication Error Reporting and Prevention (www.nccmerp.org), should be avoided.

Names That Include or Suggest the Composition of the Drug Product
Proprietary names that include or suggest the composition of the drug product may be considered misleading if the proprietary name includes or suggests the name of one or more, but not all, of its active ingredients (21 CFR 201.6(b)). In addition, a proprietary name would generally be considered misleading if it includes or suggests the name of an ingredient that is not included in the drug product.

3. Orthographic and Phonetic Similarities

When reviewing a proposed proprietary name, the Medication Error Staff within FDA's Division of Medication Error Prevention consider the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. The staff compare the spelling of the proposed proprietary name with the proprietary and established name of existing and proposed drug products because similarly spelled names may have greater likelihood to sound similar to one another when spoken, or look similar to one another when scripted.

The Medication Error Staff also examine the orthographic appearance of the proposed name using a number of different handwriting samples. Handwritten communication of product names has a long-standing association with product name confusion. Handwriting can cause similarly ***and*** dissimilarly spelled product name pairs to appear very similar to one another, which has lead to medication errors.

The Medication Error Staff apply expertise gained from root-cause analysis of such medication errors to identify sources of ambiguity within the name that could be introduced when scripting (e.g., “T” may look like “F,” lower case "a" looks like a lower case "u," etc.), along with other orthographic attributes that determine the overall appearance of the product name when scripted (see detail in Table 1 below). Additionally, since verbal communication of medication names is common in clinical settings, the Medication Error Staff compare the pronunciation of the proposed proprietary name with the pronunciation of other product names. If provided, the staff will consider an applicant’s intended pronunciation of the proprietary name. However, because an applicant has little control over how the name will be spoken in practice, the staff also consider a variety of pronunciations that could occur in the English language.

The majority of names with similarity to the proposed proprietary name can be identified through database searches. A variety of publicly available databases and resources containing product names can be used to identify similar names. The Centers use such databases, the Internet, and other printed and electronic drug product resources to search for orthographic and phonetic name similarities.

The Centers propose that applicants also conduct an extensive search to identify any existing names that are similar to the proposed proprietary name or names with orthographic and phonetic similarity to the proposed proprietary name. The examples in Table 1 should be useful in this search. It is recommended that applicants search a variety of sources and, at a minimum, search the publicly available databases listed in Appendix A. We recognize that applicants do not have access to proposed proprietary names that are in the FDA review pipeline. This limitation will be documented in the Center’s final review.

The Centers propose that applicants submit the following information with their applications:

- Search methodology employed
- Resources searched
- Pooled results with source citation and full product characteristics of each name identified as a possible source of confusion with the proposed name

Table 1:
Criteria Used to Identify Product Names that Look or Sound Similar to a Proposed Proprietary Name

Type of similarity	Considerations when searching the databases		
	Potential causes of product name similarity	**Attributes examined to identify similar product names**	**Potential Effects**
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	Names may appear similar in print or electronic media and lead to product name confusion in printed or electronic communication Names may look similar when scripted and lead to product name confusion in written communication
	Orthographic similarity	Similar spelling Length of the name Upstrokes Downstrokes Cross-stokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	Names may look similar when scripted, and lead to product name confusion in written communication
Sound-alike	Phonetic similarity	Identical prefix Identical infix Identical suffix Number of syllables Stresses Placement of vowel sounds Placement of consonant sounds Overlapping product characteristics	Names may sound similar when pronounced and lead to product name confusion in verbal communication

4. Computational Methods

To complement the above-delineated process, FDA may use a computerized method to identify any phonetic and orthographic similarities between product names. FDA recommends that applicants use such a program. Although these computerized methods are useful in hypothesis generation (i.e., developing the list of possible names that could be confused with the name

under review), they should not be used for the more complex task of hypothesis testing (i.e., evaluating which names have potential for error and harm).

There are reasons why computerized methods and algorithms are not useful for hypothesis testing. First, programs that use String-edit distance and Bigram pairs do not fully evaluate the similarity of names, particularly with respect to orthographic appearance. The lack of usefulness of the Bigram method in predicting drug name confusion is discussed in a report by Kondrak and Dorr who state that this similarity score, or Dice coefficient, is a measure that is inappropriate for estimating word similarity as it often misses similarities between words that look very much alike and have been involved in name confusion errors.[11]

Although the computerized methods and algorithms provide reproducible measures of similarity or dissimilarity, these measures are difficult to interpret when the scores reveal moderate similarities or dissimilarity between the names.

The Centers propose that applicants use computerized methods and algorithms that can detect the similarity of product names from a phonetic perspective, orthographic perspective, or both. In submitting computational data, the Centers recommend that applicants provide the following information:

- Parameters used for testing threshold
- Testing output

5. Medication Error Data

The Centers believe that data obtained from case reports of medication errors help to inform the analysis of a proposed proprietary name. The Centers search databases containing medication error reports with the goal of identifying relevant information about potential errors.

The Centers recommend that when a proposed product contains an active ingredient that is marketed domestically or abroad, all available information relevant to medication error cases associated with that active ingredient should be identified and submitted to the Centers. An applicant can obtain medication error report information from their own safety databases. Medication error report data also can be obtained from published literature, and any other relevant databases (e.g., data collected by other regulatory authorities as set forth in Appendix A).

Relevant information would include any error reports related to the product nomenclature, active ingredient, package, and/or the label and labeling. This information should be identified and reported to the Centers in line listings with a narrative as described in Box 2. This proposed data submission is consistent with the current regulations that require applicants, when filing an application, to submit a review of all information relevant to the safety of the product obtained or

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[11] Kondrak G, Dorr B. A similarity-based approach and evaluation methodology for reduction of drug name confusion. College Park (MD): University of Maryland, 2003 LAMP-TR-110, CS-TR-4549, UMIACS-TR-2003-117.

otherwise received by the applicant from any source, foreign or domestic, including information derived from any clinical or epidemiological investigations, commercial marketing experience, reports in the scientific literature, and unpublished scientific papers, as well as reports from foreign regulatory authorities that have not been previously reported to the Agency by the applicant (21 CFR 312.32(b)).

Box 2: Format for Submitting Relevant Information

- The Centers recommend that applicants submit a line listing and narratives of the medication error case reports identified in the postmarket period for marketed products with the same active ingredient as the product under review.
- The applicant should cite the source of the report along with any analysis conducted by the applicant. Applicants should submit the full text of any article published on medication errors associated with the product.
- Applicants should also categorize these errors by type (e.g., incorrect product, incorrect route of administration) using the NCC MERP taxonomy.
- Applicants should review these cases to identify factors that contributed to the medication errors and to ascertain whether these risks apply to the proposed proprietary product name. All medication error data should be integrated into the FMEA.

6. Name Simulation Studies

FDA performs simulation studies to test the response of healthcare practitioners to proposed names. However, the studies we carry out are limited. The Centers are interested in input from pharmaceutical manufacturers on the size and number of simulation studies that should be performed to create statistically reliable data. The Centers believe that the following should be considered when planning the use of simulation studies.

a. General description

Generally, name simulation studies test the response of practitioners to a proposed name by asking them to use the name in simulated real-world conditions. The more closely the simulation approximates real use conditions, the more valuable the simulation. At a minimum, certain characteristics of real use conditions are easily simulated and should be present (e.g. in the use of lined paper, prescription pads, and telephone orders to approximate inpatient written, outpatient written and outpatient verbal prescribing, respectively, and the use of background noise, different handwriting samples, different color inks, and different voices/accents to mimic the diverse prescribing conditions). Additionally, the simulation study should present the name with the corresponding product characteristics (e.g., strength, route, dosing frequency) that are likely to be used to communicate prescriptions and orders for the proposed product.

b. Study design

A simulation study designed to detect close to a zero percentage error rate with statistical significance would require an extremely large sample size (e.g., a sample of ~26,000 would be required to detect an error rate of 0.001 at the 0.05 significance level[12]). However, understanding how a proposed name will perform in real time conditions can also be accomplished through a well-designed parallel group observational study in which each group represents different prescribing scenarios based on all of the potential prescribing conditions for the proposed product (e.g., for an inpatient written order, an order written by a physician using lined paper, transcribed and entered into a computer by a unit clerk, read and dispensed by a pharmacist, read and administered by a nurse). When performing simulation testing, both quantitative and qualitative data should be collected. Both types of data can be collected anywhere in the medication use system. For example, quantitative data might document how many times a participant interpreted a prescription correctly and how many times it was misinterpreted. The qualitative data would include any concerns or problems the participants thought of or encountered while going through the process (e.g., no error occurred but a participant felt that there could have been an error in a different situation).

c. Participants

All participants in name simulation studies should be current prescribers, transcribers, dispensers, or administrators of drugs in the proposed prescribing condition for the product and should be representative of the full range of persons involved, including physicians, physician assistants, nurse practitioners, nurses, pharmacists, pharmacy technicians, ward clerks, and other individuals as needed. For example, if the product will be prescribed by private practice oncologists, the participants should include, but not be limited to, private practice oncologists. If the product will be dispensed in an inpatient setting, then the participants should include, but not be limited to, inpatient pharmacists. Consideration should be given to including primary care practitioners even when evaluating names of specialty drugs to probe what medication names outside the specialty might cause error.

d. Number of scenarios

The Centers recommend that a minimum of 20 scenarios representing each possible prescribing condition for the proposed drug be performed to provide an adequate descriptive assessment (e.g., communication from physician to ward clerk to pharmacist to nurse). Each possible prescribing condition for the proposed drug should be tested several times and each participant should only participate once (see examples Table 2 below). For example, for a drug that is administered only intravenously in an inpatient setting, an outpatient simulation using a handwritten prescription may not be helpful because this product would not be typically used in this setting of care. A simulation for an orally administered drug that could be dispensed in both in- and outpatient settings should contain all possible inpatient and outpatient scenarios. Table 2 shows example scenarios for an orally administered drug.

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12 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.

The prescription should contain the tested name embedded in a list of two to three other names of marketed drugs to mimic a real-world setting. The verbal orders should include several scenarios with an unaided pronunciation and several scenarios with a pronunciation based on how the applicant proposes to pronounce the name when marketed (e.g., "Kaletra" is pronounced by some as Kuh-let-ra and the applicant's pronunciation is Kuh-lee-tra).

Table 2:
Example Scenarios for Name Simulation Study for an Orally Administered Drug

Scenario Number	Prescribing Condition	Participant Group
1	Inpatient: Written order on lined paper	physician A - ward clerk A - pharmacist A - nurse A
2	Inpatient: Written order on lined paper	physician assistant A - ward clerk B – pharmacist B – nurse B
3	Inpatient: Written order on lined paper	physician B – nurse C – pharmacist C – nurse D
4	Inpatient: Written order on lined paper	physician C - ward clerk C –pharmacist D – nurse E
5	Inpatient: Verbal order transcribed to a written order unaided pronunciation	physician D – nurse F - ward clerk D – pharmacist E – nurse G
6	Inpatient: Verbal order transcribed to a written order unaided pronunciation	physician assistant B – nurse H - ward clerk E – pharmacist F – nurse I
7	Inpatient: Verbal order transcribed to a written order pronunciation as intended by applicant	physician E – nurse L – pharmacist G – nurse J
8	Inpatient: Verbal order transcribed to a written order pronunciation as intended by applicant	physician F – nurse N - ward clerk F – pharmacist H – nurse K
9	Inpatient: Direct computer entry	physician G - pharmacist I - nurse L
10	Inpatient: Direct computer entry	physician assistant C - pharmacist J - nurse M
11	Inpatient: Direct computer entry	physician H - pharmacist K - nurse N
12	Inpatient: Direct computer entry	nurse practitioner A - pharmacist L - nurse O
13	Outpatient: Written prescription	nurse practitioner B - pharmacist M
14	Outpatient: Written prescription	physician I - pharmacist N
15	Outpatient: Written prescription	physician J - pharmacist O
16	Outpatient: Written prescription	physician assistant D - pharmacist P
17	Outpatient: Verbal prescription left on voice mail unaided pronunciation	nurse practitioner C - pharmacist Q
18	Outpatient: Verbal prescription left on voice mail unaided pronunciation	physician K - pharmacist R
19	Outpatient: Verbal prescription left on voice mail pronunciation as intended by applicant	nurse practitioner D - pharmacist S
20	Outpatient: Verbal prescription left on voice mail pronunciation as intended by applicant	nurse practitioner E – pharmacist T
21	Outpatient: Electronic generated prescription	physician L – pharmacist U
22	Outpatient: Electronic generated prescription	physician M – pharmacy technician A – pharmacist V
23	Outpatient: Electronic generated prescription	physician assistant E – pharmacist W
	Total Participants	70

Each participant should be interviewed at the end of the simulation using nonleading scripted follow-up questions. All verbatim responses should be recorded. All qualitative data derived from follow-up questioning should be coded and analyzed based on verbatim responses from the participants (Table 3). When the results are submitted to the Centers for review, the raw data should include the coded responses as well as all the verbatim data.

Table 3:
Examples of Coded Responses to Follow-up Questions

Follow-up Questions	Coded responses	Participants with coded response
Do you think this name looks like any other drug name? If yes which drug?	Yes No Brand X Brand Y	8 52 3 5
Do you think this name sounds like any other drug name? If yes, which drug?	Yes No Brand X	8 52 8
Do you think this name looks like any medical terms or laboratory tests? If yes, what terms or tests?	Yes No	0 60
Do you think this name sounds like any medical terms or laboratory tests? If yes, what terms or tests?	Yes No	0 60
Describe your overall impression of the name. These comments do not necessarily have to be related to safety.	There are many drug names on the market that seem to start with ___. Good name does not appear to be a problem The name seems to conflict with what the drug is suppose to treat	12 35 13

Transparency of the study process is essential. Applicants should submit, and the Centers will review, all methodology associated with the simulation study—including but not limited to how participants were chosen and the composition and qualifications (e.g., current roles in clinical practice) of participants.

7. Failure Mode and Effects Analysis

Failure Mode and Effects Analysis (FMEA) is a systematic prospective method the Centers use to examine the nomenclature, labeling, and packaging for possible ways in which a failure (i.e., an error) can occur.[13] Postmarket experience has shown that the nomenclature and design of the label/labeling and packaging of a product directly contributes to the occurrence and the likelihood of medication errors.

FMEA capitalizes on the predictable and preventable nature of medication errors and enables the identification of failure modes prior to approval, when actions to overcome these issues are easier to implement than remedies available in the postapproval phase. When performing a FMEA of a proposed product, the Centers consider the use of the product at all points in the medication system.

Applicants should do the same. Because the proposed product is not yet marketed, the applicant should anticipate the use of the product under the proposed prescribing conditions by considering the intended indication and product characteristics. The applicant should then consider the proposed product in the context of the usual practice setting and work to identify potential failure modes and the effects associated with the failure modes.

a. Identifying failure modes

To identify potential failure modes, the applicant should compare the proposed proprietary name to all of the names gathered during the safety review. The applicant should consider the vulnerability of the proposed name to misinterpretation and confusion and ask the following questions:

- Could the similarity of this proposed proprietary name to other proprietary names cause the names to be confused with one another at any point under the proposed prescribing conditions?

- Are there other aspects of the proposed proprietary name, unrelated to the orthographic and phonetic similarity, that could be potentially misleading and cause confusion at any point under the proposed prescribing conditions?

Such errors may not necessarily involve confusion between the proposed drug and another drug product. For example, the Centers have learned that a proposed name for a multi-ingredient product that represents only one of the active ingredients contained in the product, names that may encode a frequency or route of administration inconsistent with the actual product characteristics, or names that look or sound like other medical terms, diagnostic tests, and abbreviations, are name characteristics that could cause confusion and lead to medication errors. A response of “yes” to either of the above questions indicates a failure mode and represents the

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[13] Joint Commission Resources, Root Cause Analysis in Healthcare 201 (3d ed, 2005).

potential for a proposed proprietary name to lead to confusion and misinterpretation. If the answer to one of these questions is "no," applicants should provide the Centers with relevant information to demonstrate that the similarity will not lead to confusion or a medication error.

b. Identifying failure effects

If the answers to the either of the aforementioned questions is "yes," the next step in the FMEA is to evaluate all potential failure modes. The potential failure modes are evaluated to determine the likely *effect* of the confusion, by asking the following question:

- Could this confusion result in medication errors in the usual practice setting?

The answer to this question is a central component of the Centers' overall risk assessment of the proposed proprietary name. If the FMEA determines that the source of confusion is unlikely to ultimately cause medication errors under the proposed prescribing conditions, the proposed name and findings should be submitted to the Centers for further review.

If the FMEA determines that the proposed proprietary name could be a source of confusion that could cause medication errors under the proposed prescribing conditions, an alternate proprietary name should be evaluated.

In certain instances, the FMEA findings may suggest other risk-reduction strategies, such as product reformulation to avoid an overlap in strength or an alternate modifier designation that may reduce the risk of medication errors resulting from product name confusion. Alternatively, the applicant may try to justify why the finding might not lead to a medication error.

c. FMEA team

Selection of the FMEA team is a critical step in the FMEA process. The team should be multidisciplinary to ensure that different perspectives and viewpoints are brought to the process. The team should include a representative sample of practicing health professionals of varying clinical backgrounds, disciplines, and experience who would be procuring, prescribing, dispensing, and administering the product under evaluation as described in Section IV.A.6.c. above. The FMEA team should include health professionals with experience in actual-use settings and members with expertise in the field of medication error prevention. FMEA teams typically consist of 8 to 12 members.[14]

The Centers will review the methodology associated with the FMEA including how the team was chosen, the composition of the team and qualifications (e.g., current roles in clinical practice) of its members, the failure modes identified, and any proposed risk mitigation strategies.

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[14] Joint Commission on Accreditation of Healthcare Organizations, Failure Mode and Effects Analysis in Health Care: Proactive Risk Reduction 27 (2005).

The step-by-step FMEA analysis, conclusions, and rationale should be submitted to the Centers as part of any proposed proprietary name submission under the pilot program.

B. Promotional Review

The Centers evaluate proposed trade names in the same manner as other promotional materials. In particular, proposed names are evaluated for claims relevant to overstatement of product efficacy, minimization of risk, broadening of product indication, unsubstantiated superiority claims, or names that are overly fanciful. See 21 U.S.C §§ 321(n), 352(a) & (n); see also 21 CFR §§ 201.10 (c), 202.1(e)(5)(i) &(e)(6)(i).

1. Evaluation

Promotional evaluation of the proposed proprietary name should focus on avoiding names that imply efficacy, risk, indication, superiority, or that are of a fanciful nature. Such evaluation should involve personnel from marketing, regulatory affairs, social scientists with expertise in consumer psychology, and legal staff to determine whether a proposed proprietary name contains misleading implications. All of these personnel should be well versed in the regulations that govern prescription product advertising and promotion and should have experience in the process of reviewing proposed promotional materials and proposed proprietary names. The analysis of sound empirical data, if available, should be given prominence in the evaluation of proposed proprietary names.

We recommend that different test personnel be used during the promotional review of the name than are used during the safety review to minimize bias during the safety review. The design and methodology used for studies that evaluate a proposed proprietary name from a promotional perspective should be valid and reliable. These studies also should be sufficiently similar to each other so as to facilitate collective evaluation at the end of the pilot program. Development of standardized, validated measures is desirable, but beyond the scope of this concept paper.[15]

2. Methodology

The Centers recommend an experimental approach to evaluate promotional implications of proposed names because this is the only method that will enable interpretation of causal relationships between variables. That is, by controlling all other factors besides the drug name, researchers can be confident that the name itself caused particular responses. Box 3 provides one possible approach for such an evaluation. Other approaches may be appropriate.

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[15] See, for example, Whitley, Jr., B.E. (1996). *Principles of research in behavioral science*. Mountain View, CA: Mayfield Publishing Company.

Box 3: Possible Evaluation Design

A ***neutral control name*** that is fictitious and pretested to ensure that it makes no representations at all (i.e., it is neutral from a promotional standpoint) should be established. This control name, having been pretested, should be used in all research on proposed names. This methodology will add control and continuity to studies.

Sponsors will use a different sample of respondents for each proposed name. The sample will respond first to questions about the neutral control name, described above. Next, half of the sample responds to the proposed name and then to an ***extreme control name*** that makes clear and extreme representations or misrepresentations about the drug. The other half of the sample responds to this extreme name first and then to the proposed name.

All control names, neutral and extreme, should be pretested to ensure that the name has the desired qualities and should be used in all research on proposed names. The extreme name will serve as a positive control to ensure that individuals can identify names that make representations about efficacy or safety. Responses to the proposed name will be compared with responses to the neutral control name.

This methodology will require a different sample for each proposed name, but will require fewer individuals per study than other designs because all subjects would see the proposed name and the two control names. In other words, this should be a within-subjects design, rather than a between-subjects design.

The approach described in Box 3 should be especially helpful in gathering information about how a name influences attitudes and behaviors of practicing healthcare providers. 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 reveal what they think they should or what they think the investigators want to hear. By comparing the compilation of responses to the proposed name with the compilation of responses to the control name, however, it could be determined whether the proposed name actually does influence these thoughts and intended behaviors. This type of study could be evaluated by looking at both the absolute percentages of participants who responded in a particular way, or by looking at the different scores between the proposed and the control name.

a. Design of Questions

A combination of open-ended and closed-ended questions, arranged from more general to more specific, should be used. The coding scheme proposed to analyze open-ended questions should be reviewed by the Centers prior to the actual coding. Questions should be designed so as to avoid leading questions, yea-saying and other forms of bias.[16] 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 many decisions about efficacy and risk are made during the IND process, the specifics may not be known at the time the proprietary name is proposed and undergoing testing. Thus, there should be a measure of participant response when they have only minimal information.

Examples of open-ended questions include:

- You have just learned of a new product named *Fungusfree*. What, if anything, does the name *Fungusfree* say or suggest to you about the product?
- Now you learn that the product *Fungusfree* is used to sterilize injection sites before inserting IV needles. What does this name mean to you in this context?

Examples of closed-ended questions include:

- How likely are you to prescribe this drug product?

  - Not at all likely
  - Somewhat likely
  - Moderately likely
  - Very likely

- On a scale from 1 to 5 where 1 equals *Strongly Disagree* and 5 equals *Strongly Agree*, please indicate your agreement or disagreement with the following statement:

  This name makes superiority claims over other products with the same indication.

b. Sampling

Note: these are general comments. A statistician should be consulted before making definitive determinations about sample size and sampling design. The size of the sample should be adequate to detect differences. The sample should represent the relevant prescribing population and be generalizable to this population. In addition, applicants should also consider testing a

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

sample of consumers. Although this group does not have prescribing authority, consumers should and do participate actively in treatment decisions. The product name may play a role here through direct-to-consumer (DTC) advertising.

c. Research Methodology

Please note that all research methodology used to support a proposed proprietary name should include the product profile provided to study participants, the complete survey questionnaire, complete results (both positive and negative), as well as any other information given to the study participants regarding the drug approval process and the regulations regarding proprietary names.

V. WHAT WILL THE CENTERS CONSIDER WHEN EVALUATING PILOT SUBMISSIONS?

This section describes the kinds of things the Centers will consider as they review manufacturers' submissions as part of the pilot program. The Centers are interested in manufacturer input on these considerations.

A. Standards

The ultimate goal of FDA's safety review is avoiding medication errors. The Centers will evaluate the safety and promotional implications of a name under the pilot program using the same methods they currently use as part of their evaluation of proposed proprietary names. If a proprietary name demonstrates vulnerability to confusion in the testing stage, the Centers will not recommend its approval for use in the market and will request the applicant propose an alternate name for evaluation. From public health and regulatory perspectives, there is no acceptable background rate for a preventable adverse drug event resulting from a medication error due to name confusion. Any preventable risk of error that can be identified prior to drug approval should be addressed. The Centers will examine both the process used and the reasoning and conclusions reached in an applicant’s determination that the name it puts forth is both safe and promotionally acceptable.

B. Assessing Adequacy of the Testing

Under the pilot program, the Centers will assess the adequacy of the data submitted to support the safety and promotional analysis. We will also identify medication error safety concerns that will need attention prior to approval. Because the Centers will also evaluate the safety and promotional aspects of the proposed name using our traditional proposed drug name review, we intend to evaluate and document the differences in the data, findings, and conclusions between the Centers' and applicant’s analyses and reviews.

Specifically, we plan to consider the following in our evaluation:

1. Did the applicant screen the proposed name with regard to the common errors listed previously (Box 1) to ensure acceptability for testing?

2. Did the applicant include a statement confirming that the proposed name does not contain a USAN stem; was the date of the search included?
3. Did the applicant conduct a thorough database search to identify existing similar names, using, at a minimum, those publicly available databases described in Appendix A? Was the search methodology adequately described, and were all resulting similar names documented?
4. Did the applicant use appropriate computational methods to identify additional look-alike and sound-alike names? Were the parameters adequately described?
5. Did the applicant consider all available medication error data related to the proposed proprietary name (e.g. for products with the same active ingredient marketed domestically or internationally)?
6. Did the applicant conduct a name simulation study that reflected all relevant real-use conditions (e.g., inpatient/outpatient, written/verbal)? Were all resulting qualitative and quantitative data from the simulation provided in addition to a clear description of the testing protocol? Was the appropriate range of practitioners included in the testing?
7. Was the composition of the FMEA team appropriate with respect to the number of people, healthcare expertise, and medication error experience? Was the FMEA analysis thorough and well-structured (e.g., were all relevant failure modes and associated effects identified, did the analysis consider all potential practice use settings, were product characteristics beyond the proprietary name considered)?
8. Were new testing methods used and were these adequately described and documented?

At the end of the pilot, FDA will evaluate the results to determine whether the model of industry conducting reviews, submitting the results to FDA, and FDA reviewing the data would be a better model than FDA conducting de novo reviews of proprietary names.

C. Increasing transparency

Although one objective of the pilot program is to increase transparency of the name evaluation and FDA review processes, in some cases the Centers have access to information that is not publicly available to applicants. The Centers will communicate with the applicant to the greatest extent possible to describe the nature of this information. Some examples include:

- Whether other names are in the Centers' review pipeline that are not in the public domain and that, in the Centers' view, may cause confusion or possible medication error. The Centers' will ***not*** release proprietary names of other applicants that are not already in the public domain.
- Whether there was postmarket experience or error risks that the applicant may have overlooked or to which the applicant did not have access.

APPENDIX A: COMPUTERIZED RESOURCES

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

Adverse Events Reporting System (AERS)

AERS is a database application in CDER that contains adverse event reports for approved drug products and therapeutic biologics. Healthcare professionals and consumers are encouraged to voluntarily report possible errors to the FDA. The main utility of such a spontaneous reporting system is to identify potential postmarket safety issues. There are inherent limitations to this system, however. For example, there is underreporting and duplicate reporting; information received may be incomplete; for any given report, there is no certainty that the reported suspect product(s) caused the reported adverse event(s); and raw counts from AERS cannot be used to calculate incidence rates or estimates of drug risk for a particular product or used for comparing risk between products.

Vaccine Adverse Event Reporting System (VAERS)

VAERS is a cooperative program for vaccine safety of the Centers for Disease Control and Prevention (CDC) and FDA. VAERS is a postmarket safety surveillance program, collecting information about adverse events that occur after the administration of U.S. licensed vaccines. The VAERS Web site provides a nationwide mechanism by which adverse events following immunization can be reported, analyzed, and made available to the public. The VAERS Web site also provides a vehicle for disseminating vaccine safety-related information to parents/guardians, healthcare providers, vaccine manufacturers, state vaccine programs, and other constituencies. The majority of VAERS reports are sent in by vaccine manufacturers and healthcare practitioners. However, these data are subject to limitations such as underreporting, simultaneous administration of multiple vaccine antigens (making it difficult to know to which of the vaccines, if any, the event might be attributed), reporting bias, and lack of incidence rates in unvaccinated comparison groups. When evaluating data from VAERS, it is important to note that for any reported event, no cause and effect relationship has been established. The report of an adverse event to VAERS is not documentation that a vaccine caused the event.

Micromedex Integrated Index

This reference contains a variety of databases covering pharmacology, therapeutics, toxicology, and diagnostics. This information will be useful for naming because it contains a large number of product names marketed both domestically and abroad.

Phonetic and Orthographic Computer Analysis (POCA)

This system was designed by the FDA. As part of the name similarity assessment, proposed names are evaluated via a phonetic/orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. Likewise, an orthographic algorithm exists that operates in a similar fashion. This product will be publicly assessable by the end of FY 2008.

Drug Facts and Comparisons, online version, St. Louis, MO

Drug Facts and Comparisons, a part of Wolters Kluwer Health, is a compendium developed for health professionals. The compendium is organized by therapeutic class; contains monographs on prescription and nonprescription products, with charts comparing similar products. (http://online.factsandcomparisons.com/index.aspx?)

Drugs@FDA

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

CBER Products

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

Electronic online version of the FDA Orange Book

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

United States Patent and Trademark Office

This website provides information regarding patent and trademarks. (http://www.uspto.gov)

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Clinical Pharmacology Online

This resource, provided by Thomson & Thomson's SAEGIS ™ Online Service, contains full monographs for the most common drugs in clinical use, plus mini monographs covering investigational, less common, combination, nutraceutical and nutritional products. It provides a keyword search engine. (www.thomson-thomson.com)

The Pharma In-Use Search Database

This database contains more than 400,000 unique pharmaceutical trademarks and trade names that are used in about 50 countries worldwide. The data are provided under license by IMS HEALTH.

Natural Medicines Comprehensive Databases

This Web site contains up-to-date clinical data on the natural medicines, herbal medicines, and dietary supplements used in the western world. (http://www.naturaldatabase.com)

Stat!Ref

STAT!Ref, is a subscription-based, online medical reference library that contains full-text information from approximately 30 texts, including tables and references. Among the database titles are: Handbook of Adverse Drug Interactions, Rudolph's Pediatrics, Basic Clinical Pharmacology and Dictionary of Medical Acronyms Abbreviations.
(http://www.statref.com)

USAN Stems

The USAN Council (tri-sponsored by the American Medical Association (AMA), the United States Pharmacopeial Convention (USP), and the American Pharmacists Association (APhA), aims for global standardization and unification of drug nomenclature and related rules to ensure that drug information is communicated accurately and unambiguously, working closely with the International Nonproprietary Name (INN) Programme of the World Health Organization (WHO), and various national nomenclature groups. This Web site, managed by the AMA, contains lists of all of the recognized USAN stems.
(http://www.ama-assn.org/ama/pub/category/4782.html)

Red Book Pharmacy's Fundamental Reference

This reference contains prices and product information for prescription, over-the-counter drugs, medical devices, and accessories.

Medical Abbreviations Book

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

APPENDIX B: PROPOSED TEMPLATE FOR A PILOT PROGRAM SUBMISSION

I. Table of Contents

II. Executive Summary

Provide a summary of the overall findings of the proprietary name review including the rational as to why the name is acceptable.

III. Introduction

a. Identify the primary and alternate proprietary name(s).

b. Provide the information required for the Center's traditional name review and/or provide the container label, carton labeling, and professional insert in an Appendix.

IV. Safety Review

a. Preliminary Screening

Describe the methods used and considerations given to the proprietary name in the prescreening process. If a proposed name fails the preliminary screening and is submitted to the Centers for evaluation, describe the rational for pursuing the name.

b. USAN Stem Search

Include a statement that indicates the name(s) does not contain a USAN stem along with the date on which this information was searched on the USAN list.

c. Orthographic and Phonetic Similarities

Describe the search methodology employed, resources searched, and pooled results with source citations. Also provide full product characteristics of each name identified as a possible source of confusion with the proposed name.

d. Computational Methods

Provide the following information on the computational method(s) used:

- Parameters used for testing threshold; and
- Testing output.

e. Medication Error Data

If your proposed product contains an active ingredient that is marketed domestically or abroad, all available information relevant to medication error cases associated with that active ingredient should be identified and submitted to the Centers. Relevant information would include any error reports related to the product nomenclature, active ingredient, package, and/or the label and labeling. This information should be identified and reported to the Centers in line listings with a narrative as described in Box 1 below.

Format for Submitting Relevant Information

- The Centers recommend that applicants submit a line listing and narratives of the medication error case reports identified in the postmarket period for marketed products with the same active ingredient as the product under review.
- The applicant should cite the source of the report along with any analysis conducted by the applicant. Applicants should submit the full text of any article published on medication errors associated with the product.
- Applicants should also categorize these errors by type (e.g., incorrect product, incorrect route of administration) using the NCC MERP taxonomy.
- Applicants should review these cases to identify factors that contributed to the medication errors and to ascertain whether these risks apply to the proposed proprietary product name. All medication error data should be integrated into the FMEA.

f. Name Simulation Studies

Describe all methodology associated with the simulation study including but not limited to how participants were chosen and the composition and qualifications of participants.

g. Failure Mode and Effects Analysis

Provide the relevant information to demonstrate that the name will not lead to confusion. Describe the methods associated with the FMEA (how the team was chosen, the composition of the team, qualification of its members, the failure modes identified, and any proposed risk mitigation strategies).

V. Promotional Review

Describe all research methodology used to support a proposed proprietary name including the product profile provided to the study participants, the complete survey questionnaire, complete results (both positive and negative), as well as any other information given to the study participants regarding the drug approval process and the regulations regarding proprietary names.

VI. Alternative Methods

If the methods used to assess the proposed proprietary name deviate from the process outlined in the formally-issued concept paper submit the rational for deviation, a full description of the methods, and all data generated and any analysis of this data from the alternative test method(s).