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RESEARCH**

APPLICATION NUMBER:

202276Orig1s000

PROPRIETARY NAME REVIEW(S)

**Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology
Office of Medication Error Prevention and Risk Management**

Proprietary Name Review

Date: April 23, 2012

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Drug Name(s) and Strength(s): Stendra (Avanafil) Tablets 50 mg, 100 mg, 200 mg

Application Type/Number: NDA 202276

Applicant/Sponsor: Vivus

OSE RCM #: 2012-597

*** This document contains proprietary and confidential information that should not be released to the public.***

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1 INTRODUCTION

This review evaluates the proposed proprietary name, Stendra, from a safety and promotional perspective. The sources and methods used to evaluate the proposed name are outlined in the reference section and Appendix A respectively.

1.1 REGULATORY HISTORY

The Applicant previously submitted the following names which were objected to for safety reasons: (b) (4) (OSE Review 2011-321, dated July 21, 2011), (b) (4) (OSE Review 2011-3054, dated November 1, 2011), and (b) (4) (OSE Review 2011-4497, dated March 1, 2012).

1.2 PRODUCT INFORMATION

The following product information is provided in the March 14, 2012 proprietary name submission.

- Active ingredient: Avanafil
- Indication of Use: Erectile dysfunction
- Route of administration: Oral
- Dosage form: Tablets
- Strength: 50 mg, 100 mg, 200 mg
- Dose and Frequency: 50 mg to 200 mg by mouth 30 minutes before sexual activity, (b) (4)
- Container and Closure systems/How Supplied: 30 and 100 count bottles
- Storage: (b) (4)

2 RESULTS

The following sections provide the information obtained and considered in the evaluation of the proposed proprietary name.

2.1 PROMOTIONAL ASSESSMENT

OPDP determined the proposed name is acceptable from a promotional perspective. DMEPA and the Division of Reproductive and Urologic Products concurred with the findings of OPDP's promotional assessment of the proposed name.

2.2 SAFETY ASSESSMENT

The following aspects of the name were considered in the overall safety evaluation.

2.2.1 *United States Adopted Names (USAN) SEARCH*

On March 15, 2012 the United States Adopted Name (USAN) stem search, identified that a USAN stem is not present in the proposed proprietary name.

2.2.2 Components of the Proposed Proprietary Name

The Applicant states in the March 14, 2012 submission that their proposed proprietary name has no derivation. The proprietary name is comprised of a single word that does not contain any components (i.e. a modifier, route of administration, dosage form, etc.) that are misleading or can contribute to medication error.

2.2.3 FDA Name Simulation Studies

Thirty-four practitioners participated in DMEPA's prescription studies. The interpretations did not overlap with or appear or sound similar to any currently marketed products. Twenty-three practitioners correctly interpreted the name. The majority of misinterpretations involved practitioners interpreting the 'd' in Stendra as a 't' (n=10). See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

2.2.4 Comments from Other Review Disciplines

In response to the OSE, April 6, 2012 e-mail, the Division of Reproductive and Urologic Products (DRUP) did not forward any comments or concerns relating to the proposed name at the initial phase of the proprietary name review.

2.2.5 Failure Mode and Effects Analysis of Similar Names

Appendix B lists possible orthographic and phonetic misinterpretations of the letters appearing in the proposed proprietary name, Stendra. Table 1 lists the names with orthographic, phonetic, or spelling similarity to the proposed proprietary name, Stendra, identified by the primary reviewer, the Expert Panel Discussion (EPD), and other review disciplines.

Table 1: Collective List of Potentially Similar Names to Stendra

Look Similar					
Name	Source	Name	Source	Name	Source
Strovite	FDA	Alimta	FDA	Treanda	FDA
Starlix	FDA	Strattera	FDA	Lusedra	FDA
Glumetza	FDA	Stalevo	FDA	StanGard	FDA
Atralin	FDA	(b) (4)	FDA	Staxyn	FDA
Sterane	FDA	Stelazine	FDA	Atridox	FDA
Atelvia	FDA	Stagesic	FDA	Staflex	FDA
Afinitor	FDA	Stimate	FDA	Temodar	FDA
Stelara	FDA	Avandia	FDA		
Sound Similar					
Extendryl	FDA				
Look and Sound Similar					
Slendra LCH	FDA	Tendra	FDA	Stendra	FDA

Our analysis of the twenty-seven names contained in Table 1 considered the information obtained in the previous sections along with their product characteristics. We determined the twenty-seven names will not pose a risk for confusion as described in Appendix D through E.

2.2.7 Communication of DMEPA's Final Decision to Other Disciplines

DMEPA communicated our findings to the Division of Reproductive and Urologic Products via e-mail on April 11, 2012. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the Division of Reproductive and Urologic Products on April 11, 2012, they stated no additional concerns with the proposed proprietary name, Stendra.

3 DISCUSSION

DMEPA acknowledges that we identified the name, 'Tendra', which only differs from the proposed proprietary name, 'Stendra' by one letter, 'S'. Based on this orthographic and phonetic similarity, DMEPA would typically communicate a denial to the Applicant due to the name being misleading because of similarity in spelling as per 21 CFR 201.10(a)(5). However, in this case, DMEPA determined that the proprietary name, 'Tendra', is a trademark from Molnlycke Healthcare for a wound care product line, and by itself, 'Tendra' does not represent a specific product. DMEPA contacted Molnlycke by phone and was told that orders for 'Tendra' would need to reference a specific product from the Molnlycke Tendra product line in order for the manufacturer to provide the correct product, such as 'Mepitel' or 'Mepilex Lite', which are two products in the Molnlycke Tendra wound care product line. Therefore, since there is no drug or wound care product marketed under the proprietary name, 'Tendra', no confusion would occur between the names 'Stendra' and 'Tendra' that could result in a medication error.

4 CONCLUSIONS

The proposed proprietary name is acceptable from both a promotional and safety perspective.

If you have further questions or need clarifications, please contact Karen Townsend, OSE project manager, at 301-796-5413.

4.1 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, Stendra, and have concluded that this name is acceptable. However, if any of the proposed product characteristics as stated in your March 14, 2012 submission are altered, DMEPA rescinds this finding and the name must be resubmitted for review. Additionally, this proprietary name must be re-evaluated 90 days prior to the approval of the application. The conclusions upon re-review are subject to change.

5 REFERENCES

1. ***Micromedex Integrated Index*** (<http://csi.micromedex.com>)

Micromedex contains a variety of databases covering pharmacology, therapeutics, toxicology and diagnostics.

2. ***Phonetic and Orthographic Computer Analysis (POCA)***

POCA is a database which was created for the Division of Medication Error Prevention and Analysis, 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 which operates in a similar fashion.

3. ***Drug Facts and Comparisons, online version, St. Louis, MO***
(<http://factsandcomparisons.com>)

Drug Facts and Comparisons is a compendium organized by therapeutic course; it contains monographs on prescription and OTC drugs, with charts comparing similar products. This database also lists the orphan drugs.

4. ***FDA Document Archiving, Reporting & Regulatory Tracking System [DARRTS]***

DARRTS is a government database used to organize Applicant and Sponsor submissions as well as to store and organize assignments, reviews, and communications from the review divisions.

5. ***Division of Medication Errors Prevention and Analysis proprietary name consultation requests***

This is a list of proposed and pending names that is generated by the Division of Medication Error Prevention and Analysis from the Access database/tracking system.

6. ***Drugs@FDA*** (<http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm>)

Drugs@FDA contains most of the drug products approved 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, generic drugs, therapeutic biological products, prescription and over-the-counter human drugs and discontinued drugs and “Chemical Type 6” approvals.

7. ***U.S. Patent and Trademark Office*** (<http://www.uspto.gov>)

USPTO provides information regarding patent and trademarks.

8. ***Clinical Pharmacology Online*** (www.clinicalpharmacology-ip.com)

Clinical Pharmacology contains full monographs for the most common drugs in clinical use, plus mini monographs covering investigational, less common,

combination, nutraceutical and nutritional products. It also provides a keyword search engine.

9. Data provided by Thomson & Thomson's SAEGIS™ Online Service, available at (www.thomson-thomson.com)

The Pharma In-Use Search database contains over 400,000 unique pharmaceutical trademarks and trade names that are used in about 50 countries worldwide. The data is provided under license by IMS HEALTH.

10. Natural Medicines Comprehensive Databases (www.naturaldatabase.com)

Natural Medicines contains up-to-date clinical data on the natural medicines, herbal medicines, and dietary supplements used in the western world.

11. Access Medicine (www.accessmedicine.com)

Access Medicine® from McGraw-Hill contains full-text information from approximately 60 titles; it includes tables and references. Among the titles are: Harrison's Principles of Internal Medicine, Basic & Clinical Pharmacology, and Goodman and Gilman's The Pharmacologic Basis of Therapeutics.

12. USAN Stems (<http://www.ama-assn.org/ama/pub/about-ama/our-people/coalitions-consortiums/united-states-adopted-names-council/naming-guidelines/approved-stems.shtml>)

USAN Stems List contains all the recognized USAN stems.

13. Red Book Pharmacy's Fundamental Reference

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

14. Lexi-Comp (www.lexi.com)

Lexi-Comp is a web-based searchable version of the Drug Information Handbook.

15. Medical Abbreviations Book

Medical Abbreviations Book contains commonly used medical abbreviations and their definitions.

16. CVS/Pharmacy (www.CVS.com)

This database contains commonly used over the counter products not usually identified in other databases.

17. Walgreens (www.walgreens.com)

This database contains commonly used over the counter products not usually identified in other databases.

18. Rx List (www.rxlist.com)

RxList is an online medical resource dedicated to offering detailed and current pharmaceutical information on brand and generic drugs.

19. Dogpile (www.dogpile.com)

Dogpile is a [Metasearch](#) engine that searches multiple search engines including Google, Yahoo! and Bing, and returns the most relevant results to the search.

APPENDICES

Appendix A

FDA's Proprietary Name Risk Assessment considers the promotional and safety aspects of a proposed proprietary name. The promotional review of the proposed name is conducted by OPDP. OPDP evaluates proposed proprietary names to determine if they are overly fanciful, so as to misleadingly imply unique effectiveness or composition, as well as to assess whether they contribute to overstatement of product efficacy, minimization of risk, broadening of product indications, or making of unsubstantiated superiority claims. OPDP provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.

The safety assessment is conducted by DMEPA. DMEPA staff search a standard set of databases and information sources to identify names that are similar in pronunciation, spelling, and orthographically similar when scripted to the proposed proprietary name. Additionally, we consider inclusion of USAN stems or other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors (i.e., dosing interval, dosage form/route of administration, medical or product name abbreviations, names that include or suggest the composition of the drug product, etc.). DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer.¹

Following the preliminary screening of the proposed proprietary name, DMEPA gathers to discuss their professional opinions on the safety of the proposed proprietary name. This meeting is commonly referred to the Center for Drug Evaluation and Research (CDER) Expert Panel discussion. DMEPA also considers other aspects of the name that may be misleading from a safety perspective. DMEPA staff conducts a prescription simulation studies using FDA health care professionals. When provided, DMEPA considers external proprietary name studies conducted by or for the Applicant/Sponsor and incorporates the findings of these studies into the overall risk assessment.

The DMEPA primary reviewer assigned to evaluate the proposed proprietary name is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name. DMEPA bases the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proprietary name and misleading nature of the proposed proprietary name with a focus on the avoidance of medication errors.

DMEPA uses the clinical expertise of its staff to anticipate the conditions of the clinical setting where the product is likely to be used based on the characteristics of the proposed product. DMEPA considers the product characteristics associated with the proposed product throughout the risk assessment because the product characteristics of the

¹ National Coordinating Council for Medication Error Reporting and Prevention.
<http://www.nccmerp.org/aboutMedErrors.html>. Last accessed 10/11/2007.

proposed may provide a context for communication of the drug name and ultimately determine the use of the product in the *usual* clinical practice setting.

Typical product characteristics considered when identifying drug names that could potentially be confused with the proposed proprietary name include, but are not limited to; established name of the proposed product, proposed indication of use, dosage form, route of administration, strength, unit of measure, dosage units, recommended dose, typical quantity or volume, frequency of administration, product packaging, storage conditions, patient population, and prescriber population. DMEPA considers how these product characteristics may or may not be present in communicating a product name throughout the medication use system. Because drug name confusion can occur at any point in the medication use process, DMEPA considers the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.² The product characteristics considered for this review appears in Appendix B1 of this review.

The DMEPA considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA compares the proposed proprietary name with the proprietary and established name of existing and proposed drug products and names currently under review at the FDA. DMEPA compares the pronunciation of the proposed proprietary name with the pronunciation of other drug names because verbal communication of medication names is common in clinical settings. DMEPA examines the phonetic similarity using patterns of speech. If provided, DMEPA will consider the Sponsor's intended pronunciation of the proprietary name. However, DMEPA also considers a variety of pronunciations that could occur in the English language because the Sponsor has little control over how the name will be spoken in clinical practice. The orthographic appearance of the proposed name is evaluated using a number of different handwriting samples. DMEPA applies expertise gained from root-cause analysis of postmarketing 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). Additionally, other orthographic attributes that determine the overall appearance of the drug name when scripted (see Table 1 below for details).

² Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006.

Table 1. Criteria Used to Identify Drug Names that Look- or Sound-Similar to a Proposed Proprietary Name.

Type of Similarity	Considerations when Searching the Databases		
	<i>Potential Causes of Drug Name Similarity</i>	<i>Attributes Examined to Identify Similar Drug Names</i>	<i>Potential Effects</i>
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	<ul style="list-style-type: none"> Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication Names may look similar when scripted and lead to drug name confusion in written communication
	Orthographic similarity	Similar spelling Length of the name/Similar shape Upstrokes Down strokes Cross-strokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	<ul style="list-style-type: none"> Names may look similar when scripted, and lead to drug 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	<ul style="list-style-type: none"> Names may sound similar when pronounced and lead to drug name confusion in verbal communication

Lastly, DMEPA considers the potential for the proposed proprietary name to inadvertently function as a source of error for reasons other than name confusion. Post-marketing experience has demonstrated that proprietary names (or components of the proprietary name) can be a source of error in a variety of ways. Consequently, DMEPA considers and evaluates these broader safety implications of the name throughout this assessment and the medication error staff provides additional comments related to the

safety of the proposed proprietary name or product based on professional experience with medication errors.

1. Database and Information Sources

DMEPA searches the internet, several standard published drug product reference texts, and FDA databases to identify existing and proposed drug names that may sound-alike or look-alike to the proposed proprietary name. A standard description of the databases used in the searches is provided in the reference section of this review. To complement the process, the DMEPA uses a computerized method of identifying phonetic and orthographic similarity between medication names. The program, Phonetic and Orthographic Computer Analysis (POCA), uses complex algorithms to select a list of names from a database that have some similarity (phonetic, orthographic, or both) to the trademark being evaluated. Lastly, DMEPA reviews the USAN stem list to determine if any USAN stems are present within the proprietary name. The individual findings of multiple safety evaluators are pooled and presented to the CDER Expert Panel. DMEPA also evaluates if there are characteristics included in the composition that may render the name unacceptable from a safety perspective (abbreviation, dosing interval, etc.).

2. Expert Panel Discussion

DMEPA gathers CDER professional opinions on the safety of the proposed product and discussed the proposed proprietary name (Expert Panel Discussion). The Expert Panel is composed of Division of Medication Errors Prevention (DMEPA) staff and representatives from the Division of Drug Marketing, Advertising, and Communications (OPDP). We also consider input from other review disciplines (OND, ONDQA/OBP). The Expert Panel also discusses potential concerns regarding drug marketing and promotion related to the proposed names.

The primary Safety Evaluator presents the pooled results of the database and information searches to the Expert Panel for consideration. Based on the clinical and professional experiences of the Expert Panel members, the Panel may recommend additional names, additional searches by the primary Safety Evaluator to supplement the pooled results, or general advice to consider when reviewing the proposed proprietary name.

3. FDA Prescription Simulation Studies

Three separate studies are conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of the proposed proprietary name with marketed U.S. drug names (proprietary and established) due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. The studies employ healthcare professionals (pharmacists, physicians, and nurses), and attempts to simulate the prescription ordering process. The primary Safety Evaluator uses the results to identify orthographic or phonetic vulnerability of the proposed name to be misinterpreted by healthcare practitioners.

In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, inpatient medication orders and/or outpatient prescriptions are written, each consisting of a combination of marketed and unapproved drug products, including the proposed name. These orders are optically

scanned and one prescription is delivered to a random sample of participating health professionals via e-mail. In addition, a verbal prescription is recorded on voice mail. The voice mail messages are then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants record their interpretations of the orders which are recorded electronically.

4. Comments from Other Review Disciplines

DMEPA requests the Office of New Drugs (OND) and/or Office of Generic Drugs (OGD), ONDQA or OBP for their comments or concerns with the proposed proprietary name, ask for any clinical issues that may impact the DMEPA review during the initial phase of the name review. Additionally, when applicable, at the same time DMEPA requests concurrence/non-concurrence with OPDP's decision on the name. The primary Safety Evaluator addresses any comments or concerns in the safety evaluator's assessment.

The OND/OGD Regulatory Division is contacted a second time following our analysis of the proposed proprietary name. At this point, DMEPA conveys their decision to accept or reject the name. The OND or OGD Regulatory Division is requested to provide any further information that might inform DMEPA's final decision on the proposed name.

Additionally, other review disciplines opinions such as ONDQA or OBP may be considered depending on the proposed proprietary name.

5. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

The primary Safety Evaluator applies his/her individual expertise gained from evaluating medication errors reported to FDA, considers all aspects of the name that may be misleading or confusing, conducts a Failure Mode and Effects Analysis, and provides an overall decision on acceptability dependent on their risk assessment of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.³ When applying FMEA to assess the risk of a proposed proprietary name, DMEPA seeks to evaluate the potential for a proposed proprietary name to be confused with another drug name because of name confusion and, thereby, cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug name confusion. FMEA allows the Agency to identify the potential for medication errors due to orthographically or phonetically similar drug names prior to approval, where actions to overcome these issues are easier and more effective than remedies available in the post-approval phase.

In order to perform an FMEA of the proposed name, the primary Safety Evaluator must analyze the use of the product at all points in the medication use system. Because the proposed product is has not been marketed, the primary Safety Evaluator anticipates the use of the product in the usual practice settings by considering the clinical and product

³ Institute for Healthcare Improvement (IHI). Failure Mode and Effects Analysis. Boston. IHI:2004.

characteristics listed in Appendix B1 of this review. The Safety Evaluator then analyzes the proposed proprietary name in the context of the usual practice setting and works to identify potential failure modes and the effects associated with the failure modes.

In the initial stage of the Risk Assessment, the Safety Evaluator compares the proposed proprietary name to all of the names gathered from the above searches, Expert Panel Discussion, and prescription studies, external studies, and identifies potential failure modes by asking:

“Is the proposed proprietary name convincingly similar to another drug name, which may cause practitioners to become confused at any point in the usual practice setting? And Are there any components of the name that may function as a source of error beyond sound/look-alike”

An affirmative answer indicates a failure mode and represents a potential for the proposed proprietary name to be confused with another proprietary or established drug name because of look- or sound-alike similarity or because of some other component of the name. If the answer to the question is no, the Safety Evaluator is not convinced that the names possess similarity that would cause confusion at any point in the medication use system, thus the name is eliminated from further review.

In the second stage of the Risk Assessment, the primary Safety Evaluator evaluates all potential failure modes to determine the likely *effect* of the drug name confusion, by asking:

“Could the confusion of the drug names conceivably result in medication errors in the usual practice setting?”

The answer to this question is a central component of the Safety Evaluator’s overall risk assessment of the proprietary name. If the Safety Evaluator determines through FMEA that the name similarity would not ultimately be a source of medication errors in the usual practice setting, the primary Safety Evaluator eliminates the name from further analysis. However, if the Safety Evaluator determines through FMEA that the name similarity could ultimately cause medication errors in the usual practice setting, the Safety Evaluator will then recommend the use of an alternate proprietary name.

Moreover, DMEPA will object to the use of proposed proprietary name when the primary Safety Evaluator identifies one or more of the following conditions in the Overall Risk Assessment:

- a. OPDP finds the proposed proprietary name misleading from a promotional perspective, and the Review Division concurs with OPDP’s findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a PROPRIETARY name or otherwise [21 U.S.C 321(n); See also 21 U.S.C. 352(a) & (n)].
- b. DMEPA identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].

- c. FMEA identifies the potential for confusion between the proposed proprietary name and other proprietary or established drug name(s), and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.
- d. The proposed proprietary name contains an USAN (United States Adopted Names) stem.
- e. DMEPA identifies a potential source of medication error within the proposed proprietary name. For example, the proprietary name may be misleading or, inadvertently, introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug and another drug product but involve a naming characteristic that when incorporated into a proprietary name, may be confusing, misleading, cause or contribute to medication errors.

If DMEPA objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the primary Safety Evaluator uses the FMEA process to identify strategies to reduce the risk of medication errors. DMEPA generally recommends that the Sponsor select an alternative proprietary name and submit the alternate name to the Agency for review. However, in rare instances FMEA may identify plausible strategies that could reduce the risk of medication error of the currently proposed name. In that instance, DMEPA may be able to provide the Sponsor with recommendations that reduce or eliminate the potential for error and, thereby, would render the proposed name acceptable.

In the event that DMEPA objects to the use of the proposed proprietary name, based upon the potential for confusion with another proposed (but not yet approved) proprietary name, DMEPA will provide a contingency objection based on the date of approval. Whichever product, the Agency approves first has the right to use the proprietary name, while DMEPA will recommend that the second product to reach approval seek an alternative name.

The threshold set for objection to the proposed proprietary name may seem low to the Applicant/Sponsor. However, the safety concerns set forth in criteria a through e above are supported either by FDA regulation or by external healthcare authorities, including the Institute of Medicine (IOM), World Health Organization (WHO), the Joint Commission, and the Institute for Safe Medication Practices (ISMP). These organizations have examined medication errors resulting from look- or sound-alike drug names, confusing, or misleading names and called for regulatory authorities to address the issue prior to approval. Additionally, DMEPA contends that the threshold set for the Proprietary Name Risk Assessment is reasonable because proprietary drug name confusion is a predictable and preventable source of medication error that, in many instances, the Agency and/or Sponsor can identify and rectify prior to approval to avoid patient harm.

Furthermore, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to rectify post-approval. Educational and other post-approval efforts are low-leverage strategies that have had limited effectiveness at alleviating medication errors involving drug name confusion. Sponsors have undertaken higher-leverage strategies, such as drug name changes, in the

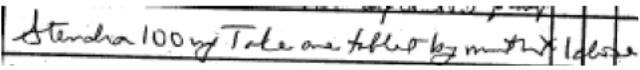
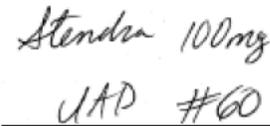
past but at great financial cost to the Sponsor and at the expense of the public welfare, not to mention the Agency’s credibility as the authority responsible for approving the error-prone proprietary name. Moreover, even after Sponsors’ have changed a product’s proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioners’ vocabulary, and as a result, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, DMEPA believes that post-approval efforts at reducing name confusion errors should be reserved for those cases in which the potential for name confusion could not be predicted prior to approval.

Appendix B: Letters with Possible Orthographic or Phonetic Misinterpretation

Letters in Name, Stendra	Scripted May Appear as	Spoken May Be Interpreted as
Upper case ‘S’	‘G’, ‘L’, ‘Z’	‘Z’, ‘F’, ‘Ch’, ‘Sh’, ‘C’
Lower case ‘t’	‘A’, ‘f’, ‘r’, ‘x’	‘d’
Lower case ‘e’	Any vowel, lower case ‘l’, lower case letter, ‘p’	Any vowel
Lower case ‘n’	‘h’, ‘m’, ‘r’, ‘u’, ‘s’, ‘x’	‘m’, ‘gn’, ‘pn’, ‘kn’
Lower case ‘d’	‘cl’, ‘ci’, ‘t’	‘b’, ‘t’
Lower case ‘r’	‘s’, ‘n’, ‘e’, ‘v’	‘w’
Lower case ‘a’	Any vowel	Any vowel

Appendix C: Prescription Simulation Samples and Results

Figure 1. Stendra Study (Conducted on March 16, 2012)

Handwritten Requisition Medication Order	Verbal Prescription
<p>Medication Order:</p> 	<p>Stendra 100 mg Use as directed #60</p>
<p>Outpatient Prescription:</p> 	

FDA Prescription Simulation Responses.

84 People Received Study		
34 People Responded		
Study Name: Stendra		
INPATIENT	VOICE	OUTPATIENT
STENDIA (1)	STENTRA (10)	STENDRA (15)
STENDRA (8)		

Appendix D: Proprietary names not likely to be confused or not used in usual practice settings for the reasons described.

Proprietary Name	Active Ingredient	Similarity to Stendra	Failure preventions
Glumetza	Metformin	Look	The pair have sufficient orthographic differences
Stelazine	Trifluoperazine	Look	The pair have sufficient orthographic differences
Stagesic	Acetaminophen and Hydrocodone	Look	The pair have sufficient orthographic differences
Staxyn	Vardenafil	Look	The pair have sufficient orthographic differences
Starflex	NA	Look	Medical device for treatment of ventricular septal defects. The pair have sufficient orthographic differences
Afinitor	Everolimus	Look	The pair have sufficient orthographic differences
Slendra LCH	Collagen Hydrolysate	Look and Sound	Foreign dietary supplement (Thailand)
	(b) (4)	Look and Sound	(b) (4)
StanGard	Stannous Fluoride	Look	Dental gel not available in the United States.
Stendra	Avanafil	Look and Sound	Identified in USPTO database by the FDA and is the proprietary name currently under review.

Appendix E: Risk of medication errors due to product confusion minimized by dissimilarity of the names and/ or use in clinical practice for the reasons described.

Proposed name: Stendra	Strength(s): 50 mg, 100 mg, 200 mg Tablets	Usual dose: 50 mg to 200 mg by mouth 30 minutes prior to sexual activity. (b) (4)
Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	Causes (could be multiple)	Prevention of Failure Mode
Tendra (Silicone Wound Care Dressing)	<u>Orthographic similarities:</u> Both names contain the letter string, 'Tendra'	Orthographic differences: Stendra begins with the letter, 'S', which will help differentiate this name pair on written orders. Marketing Status: The trademark, 'Tendra' is used to describe a product line of wound care products, each of which has a specific name, such as 'Mepilex Lite' and 'Mepitel'. Molnlycke Health Care does not have a product called, 'Tendra'.
Avandia (Rosiglitazone) 2 mg, 4 mg, 8 mg Tablets <u>Usual dose:</u> 4 mg to 8 mg by mouth daily in a single dose or two divided doses.	<u>Orthographic similarities:</u> Both names contain seven letters and are similar in length when scripted. In addition, the beginning letter, 'S' in Stendra may look similar to the beginning letter, 'A' in Avandia when scripted. Both names also share the letters, 'n', 'd', and 'a' in similar positions. <u>Product characteristics:</u> Dosage form: Tablet Route of administration: Oral	Orthographic differences: Stendra contains three upstroke letters, 'S', 't', and 'd', giving it a different shape when scripted compared to the two upstroke letters, 'A' and 'd' in Avandia. Frequency of administration: 30 minutes prior to sexual activity. (b) (4) or Use as directed (UAD) vs. once a day or twice a day Strength/Dose: Multiple strengths (50 mg, 100 mg, 200 mg vs. 2 mg, 4 mg, 8 mg) with no overlapping strengths or doses.

<p>Strovite (Folic Acid, Vitamin B1, Vitamin B2, Vitamin B3, Vitamin B5, Vitamin B6, Vitamin C)</p> <p>0.5 mg/20 mg/10 mg/ 100 mg/20 mg/5 mg/ 500 mg Tablets</p> <p><u>Usual dose:</u> Take one tablet by mouth once a day.</p>	<p><u>Orthographic similarities:</u> <i>Both names begin with the letters, ‘St’, and share the letters ‘r’ and ‘e’. Both names are also similar in length when scripted (7 vs 8 letters).</i></p> <p><u>Product characteristics:</u> Dosage form: Tablet</p> <p>Route of administration: Oral</p> <p>Numerical overlapping strength: ‘100 mg’</p>	<p>Orthographic differences: The third upstroke letter, ‘d’, in Stendra, is in a different position than the third upstroke letter, ‘t’ in Strovite, giving it a different shape when scripted.</p> <p>Frequency of Administration: 30 minutes prior to sexual activity. (b) (4) or Use as directed (UAD) vs. once a day</p>
<p>Starlix (Nateglinide)</p> <p>60 mg and 120 mg Tablets</p> <p><u>Usual dose:</u> 60 mg to 120 mg by mouth three times a day before meals.</p>	<p><u>Orthographic similarities:</u> <i>Both names begin with the letters, ‘St’ and share the letters, ‘r’ and ‘a’. In addition, both names contain seven letters and are similar in length when scripted. Both names also have three upstroke letters, (‘S’, ‘t’, ‘d’ vs. ‘S’, ‘t’, ‘l’), in similar positions, giving them a similar shape when scripted.</i></p> <p><u>Product characteristics:</u> Dosage form: Tablet</p> <p>Route of administration: Oral</p>	<p>Orthographic differences: The ending letters, ‘ix’ in Starlix look different when scripted from the ending letters, ‘ra’ in Stendra.</p> <p>Frequency of Administration: 30 minutes prior to sexual activity (b) (4) or Use as directed (UAD) vs. three times a day before meals</p> <p>Strength: Both products have multiple strengths (50 mg, 100 mg, 200 mg vs. 60 mg, 120 mg) with no numerical strength or dose overlap.</p>

<p>Atralin (Tretinoin) 0.05% Gel</p> <p><u>Usual dose:</u> Apply a thin layer to affected area once a day at bedtime.</p>	<p><u>Orthographic similarities:</u> <i>Both names contain seven letters and are similar in length when scripted. They also have three upstroke letters, ('S', 't', 'd' vs. 'A', 't', 'l') in similar positions making the names similar in shape when scripted. In addition, both names have the letter, 't' in the second position and share the letters, 'n', 'r', and 'a'.</i></p>	<p>Orthographic differences: The position of the letters, 'r' and 'n' in Stendra are very different from their positions in Atralin, providing some orthographic differentiation between the name pair when scripted.</p> <p>Strength: Multiple (50 mg, 100 mg, 200 mg) vs. Single (0.05%)</p>
<p>Sterane (Prednisone) 5 mg Tablets</p> <p><u>Usual dose:</u> One tablet by mouth once a day with food.</p>	<p><u>Orthographic similarities:</u> <i>Both names contain seven letters and are similar in length when scripted. In addition, both names begin with the letters, 'Ste' and share the letters, 'r', 'n' and 'a'.</i></p> <p><u>Product characteristics:</u></p> <p>Dosage form: Tablet</p> <p>Route of administration: Oral</p>	<p>Orthographic differences: Stendra has three upstroke letters, 'S', 't', and 'd', giving it a different shape when scripted compared to the two upstroke letters, 'S' and 't' in Sterane.</p> <p>Frequency of Administration: 30 minutes prior to sexual activity. (b) (4) or Use as directed (UAD) vs. once a day</p>
<p>Stelara (Ustekinumab) 45 mg/0.5 mL, 90 mg/1 mL Injection</p> <p><u>Usual dose:</u> 45 mg or 90 mg injected subcutaneously every 4 to 12 weeks.</p>	<p><u>Orthographic similarities:</u> <i>Both names contain seven letters and are similar in length when scripted. In addition, both names begin with the letters, 'Ste' and share the letters, 'ra' in the same positions.</i></p>	<p>Frequency of Administration: 30 minutes prior to sexual activity. (b) (4) or Use as directed (UAD) vs. one injection every 4 to 12 weeks</p> <p>Strength: Multiple (50 mg, 100 mg, 200 mg) vs. (45 mg and 90 mg) with no overlap</p>

<p>Stimate (Desmopressin) 150 mcg/actuation Nasal Spray</p> <p><u>Usual dose:</u> One spray in each nostril. Dose may be repeated in 8 to 24 hours. If given preoperatively, administer 2 hours before surgery.</p>	<p><u>Orthographic similarities:</u> <i>Both names contain seven letters and are similar in length when scripted. In addition, both names begin with the letters, 'St' and share the letters, 'e' and 'a'.</i></p>	<p>Frequency of Administration: 30 minutes prior to sexual activity. (b) (4) or Use as directed (UAD) vs. prior to surgery or in two doses 8 to 24 hours apart.</p> <p>Strength: Multiple (50 mg, 100 mg, 200 mg) vs. (150 mcg/actuation) with no overlap</p>
<p>Atridox (Doxycycline Hyclate) 50 mg Extended Release Periodontal System</p> <p><u>Usual dose:</u> 50 mg administered subgingivally every 4 months</p>	<p><u>Orthographic similarities:</u> <i>Both names contain seven letters and are similar in length when scripted. In addition, the beginning letter, 'S' in Stendra may look similar to the beginning letter, 'A' in Atridox and both names share the letters, 't', 'r', and 'd'.</i></p> <p><u>Product Characteristics:</u> Strength: 50 mg</p>	<p>Orthographic differences: The ending letters, 'ra' in Stendra look different from the ending letters, 'ox' in Atridox when scripted.</p> <p>Frequency of Administration: 30 minutes prior to sexual activity. (b) (4) or Use as directed (UAD) vs. every 4 months</p> <p>Setting of Use: Ambulatory care setting for self-administration vs. dental clinic setting for administration by a licensed dentist or technician.</p>
<p>Atelvia (Risedronate Sodium) 35 mg Tablets</p> <p><u>Usual dose:</u> One tablet by mouth once a week in the morning immediately following breakfast with at least 4 ounces of water.</p>	<p><u>Orthographic similarities:</u> <i>Both names contain 7 letters and are similar in length and shape when scripted. Both names also have the letters, 't' and 'e' in the second and third positions in the names and share the letter, 'a'.</i></p> <p><u>Product characteristics:</u> Dosage form: Tablet Route of administration: Oral</p>	<p>Orthographic differences: The spacing of the upstroke letters, 't' and 'd' in Stendra is greater (due to the intervening letters, 'en') than the spacing of the corresponding upstroke letters, 't' and 'l' in Atelvia, which are separated by the single letter, 'e'. This provides some orthographic differentiation.</p> <p>Frequency of Administration: 30 minutes prior to sexual activity. (b) (4) or Use as directed (UAD) vs. once a week</p>

<p>Alimta (Pemetrexed) 100 mg and 500 mg for Injection</p> <p><u>Usual dose:</u> 500 mg/m² intravenously over 10 minutes on days 1 through 21 of cycle.</p>	<p><u>Orthographic similarities:</u> <i>Both names are similar in length when scripted, (7 vs. 6 letters) and contain three upstroke letters, ('S', 't', 'd' vs. 'A', 'l', 't'), giving them a similar shape when scripted. The names also share the letters, 't' and 'a'. In addition, the beginning letter, 'S' in Stendra may look similar to the beginning letter, 'A' in Alimta when scripted.</i></p> <p><u>Product characteristics:</u></p> <p>Numerical overlapping strengths: 100 mg</p>	<p>Orthographic differences: The location of the cross letter, 't' in Stendra is in the second position compared to being in the sixth position in Alimta.</p> <p>Frequency of Administration: 30 minutes prior to sexual activity. (b) (4) or Use as directed (UAD) vs. once a day for 21 days of cycle.</p>
<p>Strattera (Atomoxetine) 10 mg, 18 mg, 25 mg, 40 mg, 60 mg, 80 mg, 100 mg Capsules</p> <p><u>Usual dose:</u> One capsule by mouth once or twice a day not to exceed 100 mg per day.</p>	<p><u>Orthographic similarities:</u> <i>Both names begin with the letters, 'St' and share the letters, 'r', 'e', and 'a'.</i></p> <p><u>Product characteristics:</u></p> <p>Dosage form: Oral solid</p> <p>Route of administration: Oral</p>	<p>Orthographic differences: Stendra contains three upstroke letters, 'S', 't', 'd' and has a different shape when scripted compared to four upstroke letters, 'S', 't', 't', 't', in Strattera.</p> <p>Frequency of administration: 30 minutes prior to sexual activity. (b) (4) or Use as directed (UAD) vs. once or twice a day.</p>

<p>Stalevo (Carbidopa, Levodopa, Entacapone) 50 mg, 75 mg, 100 mg, 125 mg, 150 mg, 200 mg Tablets</p> <p><u>Usual dose:</u> One tablet by mouth once a day</p>	<p><u>Orthographic similarities:</u> <i>Both names contain seven letters and are similar in length when scripted. In addition, both names begin with the letters, ‘St’ and share the letters, ‘a’ and ‘e’.</i></p> <p><u>Product characteristics:</u></p> <p>Dosage form: Tablet</p> <p>Route of administration: Oral</p> <p>Strength: 100 mg and 200 mg</p>	<p>Orthographic differences: The ending letters, ‘dra’ in Stendra, look different from the ending letters, ‘evo’ in Stalevo when scripted.</p> <p>Frequency of administration: 30 minutes prior to sexual activity. (b) (4) or Use as directed (UAD) vs. once or twice a day.</p>
<p>Treanda (Bendamustine) 25 mg and 100 mg for Injection</p> <p><u>Usual dose:</u> 60 mg/m² to 120 mg/m² intravenously infused daily over a 21 or 28 day cycle depending on the indication.</p>	<p><u>Orthographic similarities:</u> <i>Both names contain seven letters and are similar in length when scripted. In addition, both names share the letters, ‘t’, ‘r’, ‘e’, ‘n’, ‘d’ and ‘a’.</i></p> <p><u>Product characteristics:</u></p> <p>Strength: 100 mg</p> <p>Dose: 100 mg, 200 mg</p>	<p>Orthographic differences: Stendra has three upstroke letters, ‘S’, ‘t’, ‘d’, giving it a different shape when scripted compared to the two upstroke letters, ‘T’ and ‘d’ in Treanda.</p> <p>Frequency of administration: 30 minutes prior to sexual activity. (b) (4) or Use as directed (UAD) vs. once a day</p>
<p>Lusedra (Fospropofol) 35 mg/1 mL Injection</p> <p><u>Usual dose:</u> 70 mg to 437.5 mg intravenously for sedation</p>	<p><u>Orthographic similarities:</u> <i>Both names contain seven letters and are similar in length when scripted. In addition, both names end in the letters, ‘dra’. and share the letters, ‘e’ and ‘s’.</i></p> <p><u>Product characteristics:</u></p> <p>Potential overlapping doses: 100 mg, 200 mg</p>	<p>Orthographic differences: Stendra contains three upstroke letters, ‘S’, ‘t’, and ‘d’, giving it a different shape when scripted compared to the two upstroke letters, ‘L’ and ‘d’ in Lusedra. In addition, Stendra has the cross stroke letter, ‘t’ in the second position which Lusedra does not have.</p> <p>Frequency of administration: 30 minutes prior to sexual activity. (b) (4) or Use as directed (UAD) vs. as needed for sedation</p> <p>Setting of Use: Lusedra is administered by licensed anesthesiologists in an inpatient and/or surgical setting whereas Stendra will be used in an ambulatory care (retail pharmacy setting) primarily.</p>

<p>Temodar (Temozolomide) 5 mg, 20 mg, 100 mg, 140 mg, 180 mg, 250 mg Capsules 100 mg Injection</p> <p><u>Usual dose:</u></p> <p><i>Oral:</i> 75 mg/m² to 250 mg/m² once a day for 5 to 42 days depending on the indication.</p> <p><i>Parenteral:</i> 75 mg/m² to 200 mg/m² intravenously over 90 minutes daily on days 1 to 5 of a 28 day cycle.</p>	<p><u>Orthographic similarities:</u> <i>Both names contain seven letters and are similar in length when scripted. In addition, both names share the letters, ‘t’, ‘e’, ‘d’, ‘a’, and ‘r’.</i></p> <p><u>Product characteristics:</u> Strength: 100 mg</p>	<p>Orthographic differences: The letter string, ‘end’ in Stendra looks different from the corresponding letter string, ‘mod’ in Temodar when scripted.</p> <p>Frequency of administration: 30 minutes prior to sexual activity. (b) (4) or Use as directed (UAD) vs. once a day</p>
<p>Extendryl (Chlorpheniramine; Methscopolamine; Phenylephrine) 2 mg/1.25 mg/10 mg Chewable Tablet 2 mg/1.25 mg/10 mg/ 5 mL Syrup</p> <p><u>Usual dose:</u></p> <p><i>Chewable Tablet:</i> Chew one to two tablets by mouth every 4 hours as needed.</p> <p><i>Syrup:</i> Take one to two teaspoonsful by mouth every 4 hours as needed.</p>	<p><u>Phonetic similarities:</u> <i>Both names contain the letter string, ‘endr’ which sounds identical in both names when spoken. In addition, the beginning letters, ‘St’ in Stendra, sound similar to the beginning letters, ‘Ext’ in Extendryl. The endings of both names, ‘ra’ vs. ‘ryl’ also sound similar.</i></p> <p><u>Product characteristics:</u> Dosage form: Tablet Route of Administration: Oral</p>	<p>Phonetic differences: Stendra contains two syllables compared to Extendryl which contains three syllables.</p> <p>Frequency of administration: 30 minutes prior to sexual activity. (b) (4) or Use as directed (UAD) vs. every 4 hours as needed.</p> <p>Strength: Multiple (50 mg, 100 mg, 200 mg) vs. Single (2 mg/1.25 mg/10 mg) with no strength overlap.</p>

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