CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

204308Orig1s000

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--Final

Date:	July 3, 2013
Reviewer(s):	Sue (Liu) Liu, PharmD Division of Medication Error Prevention and Analysis
Team Leader	Irene Z. Chan, PharmD, BCPS Division of Medication Error Prevention and Analysis
Drug Name(s) and Strength(s):	Epaned (Enalapril Maleate) Powder for Oral Solution 1 mg/mL (after reconstitution)
Application Type/Number:	NDA 204308
Applicant/sponsor:	Silvergate Pharmaceuticals, Inc.
OSE RCM #:	# 2013-1488

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1 INTRODUCTION

This re-assessment of the proposed proprietary name, Epaned is written in response to the anticipated approval of this NDA within 90 days from the date of this review. DMEPA found the proposed name, Epaned, acceptable in OSE Review 2013-683 dated June 7, 2013.

2 METHODS AND DISCUSSION

For re-assessments of proposed proprietary names, DMEPA searches a standard set of databases and information sources (see section 4) to identify names with orthographic and phonetic similarity to the proposed name that have been approved since the previous OSE proprietary name review. For this review we used the same search criteria described in OSE Review 2013-683. We note our previous review did not consider the complete dosage range and frequency of Epaned, up to 40 mg in a single or divided dose. Therefore, we re-evaluated the previously identified names (see OSE Review 2013-683 dated June 7, 2013). Our re-assessment did not alter our previous conclusion regarding the acceptability of the proposed proprietary name. In addition, the searches of the databases yielded three new names ((b) (4) , thought to look or sound similar to Epaned and represent a potential source of drug name confusion. Failure mode and effects analysis was applied to determine if the proposed proprietary name could potentially be confused with Epaned and lead to medication errors. This analysis determined that the name similarity between Epaned and the identified names was unlikely to result in medication error for the reasons presented in Appendices A and B.

Additionally, DMEPA searched the USAN stem list to determine if the name contains any USAN stems as of the last USAN updates. The Safety Evaluator did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of July 2, 2013.

3 CONCLUSIONS

The re-evaluation of the proposed proprietary name, Epaned, did not identify any vulnerability that would result in medication errors with any additional name(s) noted in this review. Thus, DMEPA has no objection to the proprietary name, Epaned, for this product at this time.

DMEPA considers this a final review; however, if approval of the NDA is delayed beyond 90 days from the date of this review, the Office of DNP should notify DMEPA because the proprietary name must be re-reviewed prior to the new approval date.

If you have further questions or need clarifications, please contact Cherye Milburn, OSE project manager, at 301-796-2084.

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4 REFERENCES

1. OSE Review 2013-683 dated June 7, 2013.

2. ***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.

3. ***USAN Stems*** *(http://www.ama-assn.org/ama/pub/physician-resources/medical-science/united-states-adopted-names-council/naming-guidelines/approved-stems.page?)*

   USAN Stems List contains all the recognized USAN stems.

4. ***Division of Medication Error Prevention and Analysis Proprietary Name Consultation Request***

   Compiled list of proposed proprietary names submitted to the Division of Medication Error Prevention and Analysis for review. The list is generated on a weekly basis from the Access database/tracking system.

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

Proprietary Name	Active Ingredient	Similarity to Epaned	Failure Preventions
(b) (4)	Levonorgestrel and Ethinyl Estradiol	Look	Proprietary name found unacceptable in OSE RCM 2010-2107 and 2010-2109. Product approved under the established name (ANDA 091663)
	Clonidine	Look	Product approved under the established name (NDA 22500 and 22499)

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

No	Proposed name: Epaned **Dosage Form(s):** Powder for oral solution **Strength(s):** 1 mg/mL (after reconstitution) **Usual Dose:** Hypertension: The recommended initial dose is 5 mg once a day. Titrate upward to maximum of 40 mg daily as needed to help achieve blood pressure goals. The dose may be divided and administered twice daily if the antihypertensive effect diminishes at the end of the dosing interval. *Use with diuretics* The recommended initial dose in patients taking diuretics is 2.5 mg daily Dosage Adjustment in Hypertensive Patients with Renal Impairment: Normal or mild: 5 mg/day (Initial) Moderate to severe: 2.5 mg/day (Initial) Dialysis: 2.5 mg on dialysis days (Initial) The dosage may be titrated upward as needed to a maximum of 40 mg daily. Pediatric Hypertensive Patients: The usual recommended starting dose is 0.08 mg/kg (up to 5 mg) once daily. Dosage should be adjusted according to blood pressure response. Doses above 0.58 mg/kg (or in excess of 40 mg) have not been studied in pediatric patients.	**Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion** **Causes (could be multiple)**	**Prevention of Failure Mode** **In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names**
1.			(b) (4)

	(b) (4)

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/s/

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07/03/2013

IRENE Z CHAN
07/03/2013

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:	June 7, 2013
Reviewer(s):	Sue (Liu) Liu, PharmD Division of Medication Error Prevention and Analysis
Team Leader	Irene Z. Chan, PharmD, BCPS Division of Medication Error Prevention and Analysis
Division Director	Carol Holquist, Rph Division of Medication Error Prevention and Analysis
Drug Name and Strength:	Epaned (Enalapril Maleate) Powder for Oral Solution 1 mg/mL (after reconstitution)
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CONTENTS

1 INTRODUCTION

This review evaluates the proposed proprietary name, Epaned, 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

DMEPA previously evaluated the proposed proprietary name (b) (4) for this NDA under OSE RCM #2012-1911. On October 17, 2012, DMEPA held a teleconference with the Applicant to inform the Applicant of our preliminary concerns with the proposed proprietary name, (b) (4), due to it containing a significant portion of the established name. On October 23, 2012, the Applicant formally withdrew the Request for Proprietary Name Review of (b) (4).

The Applicant subsequently submitted proposed proprietary name, (b) (4), on January 15, 2013. OPDP found the name, (b) (4) unacceptable from a promotional perspective. The Applicant was notified of this decision by letter on March 1, 2013.

1.2 PRODUCT INFORMATION

The following product information is provided in the March 13, 2013 proprietary name submission.

- Active Ingredient: Enalapril maleate
- Indication of Use: Treatment of hypertension in pediatric patients (b) (4) of age.
- Route of Administration: Oral
- Dosage Form: Powder for Oral Solution
- Strength: Powder for Oral Solution contains 150 mg of enalapril maleate in a 150 mL bottle. Reconstitution with 150 mL of ORA-SWEET® SF results in a 1 mg/mL oral solution.
- Dose and Frequency: The usual recommended starting dose is 0.08 mg/kg (up to 5 mg) once daily. Dosage should be adjusted according to blood pressure response.
- How Supplied and Container and Closure Systems: Epaned is supplied as a kit.
    - One 150 mL bottle contains 150 mg of enalapril maleate powder for oral solution in an HDPE bottle with child-resistant cap to provide 150 mg of enalapril maleate per bottle.
    - One 150 mL bottle of Ora-Sweet SF.
- Storage: Store dry powder at controlled room temperature 15°C to 30°C (59°F to 86°F). Store reconstituted oral solution at room temperature 15°C to 30°C (59°F to 86°F) for no longer than 60 days. Do not freeze. Keep container tightly closed. Protect from moisture.

2 RESULTS

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

2.1 PROMOTIONAL ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined the proposed name is acceptable from a promotional perspective. DMEPA and the Division of Cardiovascular and Renal Products (DCRP) concurred with the findings of OPDP's promotional assessment of the proposed name.

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) SEARCH

The March 26, 2013 search of the United States Adopted Name (USAN) stems did not identify that a USAN stem is present in the proposed proprietary name.

2.2.2 Components of the Proposed Proprietary Name

The Applicant indicated in their submission that the proposed name, Epaned, is not derived from any one particular concept. This 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

Forty four practitioners participated in DMEPA's prescription studies. The interpretations did not overlap with any currently marketed products nor did the misinterpretations sound or look similar to any currently marketed products or any products in the pipeline. Of the inpatient and outpatient written studies, 27 of 32 participants interpreted the name Epaned correctly. However various misinterpretations in verbal prescriptions occurred including misinterpretation of the 'd' as 't'. We have considered these variations in our look-alike and sound-alike searches and analysis. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

2.2.4 Comments from Other Review Disciplines at Initial Review

In response to the OSE, March 22, 2013 e-mail, the Division of Cardiovascular and Renal Products (DCRP) raised concerns that Epaned "has a similar sound to Epinep (short for epinephrine) and epinephrine" at the initial phase of the proprietary name review. We evaluated the potential for confusion between Epaned and Epinep or Epinephrine (see Appendix E).

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, Epaned. Table 1 lists the names with

orthographic, phonetic, or spelling similarity to the proposed proprietary name, Epaned identified by the primary reviewer (PR), the Expert Panel Discussion (EPD), and other review disciplines (DCRP).

Table 1: Collective List of Potentially Similar Names (DMEPA, EPD, and Other Disciplines)

Look Similar (n=39)							
Name	***Source***	***Name***	***Source***	***Name***	***Source***	***Name***	***Source***
Episil	EPD	Apurol	PR	Epovar	PR	Eryped	EPD
Emend	EPD	Epivir	PR	Epimax	PR	Egifta	EPD
Opana	EPD	Aquoral	PR	(b) (4) ***	PR	Epazote	EPD
Exparel	EPD	Eperbel-S	PR	(b) (4) ***	EPD	(b) (4) ***	EPD
Eye-sed	EPD	Elavil	PR	Enovid	PR	Hepacid	PR
Apacet	EPD	Clomid	PR	Eprinex	PR	Opromed	PR
Agoral	EPD	Fluonid	PR	Opasal	PR	(b) (4) ***	PR
Aquanil	EPD	Alomide	PR	Aprinol	PR	(b) (4) ***	PR
Epinal	EPD	Equi-cet	PR	Epitol	EPD	(b) (4) ***	PR
(b) (4) ***	EPD	Epivar	PR	Aquasol A	EPD		
Sound Similar (n=9)							
Name	***Source***	***Name***	***Source***	***Name***	***Source***	***Name***	***Source***
Atamet	PR	Epinephrine	EPD/DCRP	(b) (4) ***	PR		
Obenix	PR	Iberet-Folic-500	PR	Ebon-Aide	PR		
Abelcet	PR	(b) (4) ***	PR	(b) (4) ***	PR		
Look and Sound Similar (n=6)							
Name	***Source***	***Name***	***Source***	***Name***	***Source***	***Name***	***Source***
Epipen	EPD	Equanil	EPD	Apamead	PR		
Epimide-50	EPD	(b) (4)	PR	(b) (4) ***	EPD		

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Our analysis of the 54 names contained in Table 1 considered the information obtained in the previous sections along with their product characteristics. We determined all 54 names will not pose a risk for confusion as described in Appendices D through E.

2.2.6 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to DCRP via e-mail on April 18, 2013. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the DCRP on April 25, 2013, they stated no additional concerns with the proposed proprietary name, Epaned.

3 CONCLUSIONS

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

If you have further questions or need clarifications, please contact, OSE project manager Cherye Milburn, at 301-796- 2084.

3.1 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, Epaned, and have concluded that this name is acceptable.

The proposed proprietary name must be re-reviewed 90 days prior to approval of the NDA. The results are subject to change. If any of the proposed product characteristics as stated in your March 13, 2013 submission are altered, the name must be resubmitted for review.

4 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 (www.thomsonhc.com/home/dispatch)***

    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 (www.medilexicon.com)***

    Medical Abbreviations dictionary 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.

20. ***Natural Standard (http://www.naturalstandard.com)***

    Natural Standard is a resource that aggregates and synthesizes data on complementary and alternative medicine.

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 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.

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

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 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**		
	Potential Causes of Drug Name Similarity	*Attributes Examined to Identify Similar Drug 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 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	• 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	• 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 gather 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 Office of Prescription Drug Promotion (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 Section 1.2 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 posses 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

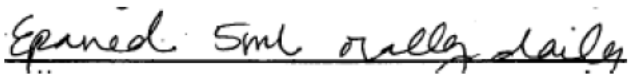
past but at great financial cost to the Sponsor and at the expense of the public welfare, not to mention the Agency's credibility as the authority responsible for approving the error-prone proprietary name. Moreover, even after Sponsors' have changed a product's proprietary name in the post-approval 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 and Letter Strings with Possible Orthographic or Phonetic Misinterpretation

Letters in Name, Epaned	Scripted May Appear as	Spoken May Be Interpreted as
Capital 'E'	C, f, Ex	Any vowel
Lower case 'e'	a, i, l, o, u, p	Any vowel
Lower case 'p'	yn, ys, g, j, l, q	b, pp
Lower case 'a'	el, ce, ci, cl, d, o, u	Any vowel
Lower case 'n'	m, u, x, r, rr, h, s, v	dn, gn, kn, mn, pn, m
Lower case 'e'	a, i, l, o, u, p	Any vowel, en
Lower case 'd'	cl, ci, l, a	b, t
Letter Strings		
An	cur, w	

Appendix C: Prescription Simulation Samples and Results

Figure 1. Epaned Study (Conducted on 3/21/13)

Handwritten Requisition Medication Order	Verbal Prescription
Medication Order: 	Epaned Take 5 mL by mouth daily

Outpatient Prescription: Epaned Take 5mL by mouth daily #150 mL	#150 mL

FDA Prescription Simulation Responses (Aggregate 2 Rx Studies Report)

Study Name: Epaned

As of Date 3/26/2013

190 People Received Study
44 People Responded

Study Name: Epaned

INPATIENT	VOICE	OUTPATIENT
EPANED (13)	APPENET (1)	EPAMED (3)
EXPANED (1)	EBENID (1)	EPANED (14)
	EPINED (2)	EPANEL (1)
	EPINENT (1)	
	EPINET (1)	
	EPINID (5)	
	EPINIT (1)	

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

No.	Proprietary Name	Active Ingredient	Similarity to Epaned	Failure preventions
1.	Epitol	Carbamazepine	Look	The name pair has sufficient orthographic differences.
2.	Aquasol A	Vitamin A Palmitate	Look	The name pair has sufficient orthographic differences.
3.	Eryped	Erythromycin Ethylsuccinate	Look	The name pair has sufficient orthographic differences.
4.	Egrifta	Tesamorelin Lyophilisate	Look	The name pair has sufficient orthographic differences.
5.	Epazote	Chenopodium Oil	Look	The name pair has sufficient orthographic differences.

6.	(b) (4)			
7.	(b) (4) ***	Enalapril maleate	Both	Applicant withdrew (b) (4) *** and submitted Epaned, which is the subject of this review.
8.	Hepacid	Alkyl dimethyl benzyl ammonium chloride 0.07%	Look	This is not a pharmaceutical product (Disinfectant). It would not be ordered by prescription.
9.	Opromed	Homeopathic product	Both	Found in Natural Medicines database. Dosing information cannot be found in other commonly used databases.
10.	Ebon-Aid		Sound	US Trademark. This is not a pharmaceutical product (bandages for skin wounds).
11.	(b) (4)			
12.				
13.				
14.	Apamead	Amobarbital, aspirin, dextroamphetamine sulfate, phenacetin	Both	Product found in Micromedex. Dosing information cannot be found in other commonly used databases.
15.	Opasal	Acetaminophen, Phenylpropanolamine	Look	Found in Micromedex databases with statement product is discontinued due to FDA advisory to remove phenylpropanolamine containing products be removed from market.
16.	(b) (4)			

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17.	Aprinol	Leptogluterin-B, acetylsalicylic acid, caffeine, ephedrine alkaloid	Look	Product discontinued by manufacturer since FDA banned ephedra-containing products in the US.
18.	(b) (4)	Carbinoxamine maleate	Sound	ODPD objected to name in OSE review 2011-429. NDA 022556 is approved under name Karbinal ER
19.		Carbinoxamine maleate	Sound	ODPD objected to alternate name in OSE review 2011-429. NDA 022556 is approved under name Karbinal ER
20.	Eprinex	Eprinomectin	Look	Found in POCA and Dogpile databases. This is a veterinary product.
21.	Iberet-Folic-500	Ascorbic Acid, Calcium Pantothenate, Cyanocobalamin, Ferrous Sulfate, Folic Acid, Niacinamide, Pyridoxine, Riboflavin, Thiamine Mononitrate	Sound	The name pair has sufficient phonetic differences.
22.	(b) (4)	Epinephrine	Look	Product approved as Auvi-Q.

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.

No	**Proposed name:** Epaned **Dosage Form(s):** Powder for oral solution **Strength(s):** 1 mg/mL (after reconstitution) **Usual Dose:** The usual recommended	**Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion** **Causes (could be multiple)**	**Prevention of Failure Mode** **In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names**

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	starting dose is 0.08 mg/kg (up to 5 mg) once daily. Dosage adjusted according to blood pressure response Kit containing one 150 mL bottle with 150 mg enalapril maleate powder for oral solution in a HDPE bottle with a child-resistant cap to provide 150 mg of enalapril maleate per bottle and one150 mL bottle of Ora-Sweet SF.		
1.	Emend (Aprepitant) Capsule; (Fosaprepitant Dimeglumine) Injection Strength: Capsule: 40 mg, 80 mg, 125 mg Injection: 115 mg and 150 mg Dose: Capsule: 125 mg orally 1 hour prior to chemotherapy treatment (Day 1) and 80 mg orally once daily in the morning on Days 2 and 3, or 40 mg within 3 hours to induction of anesthesia. Injection: 150 mg via intravenous infusion on Day 1, or 115 mg	Orthographic: Both begin with the letter 'E' and end with the letter 'd.' The 'a' at the 3rd position in Epaned looks similar to the 'e' at the 3rd position in Emend. Both contain the letter 'n' at the 4th position. Route: Emend and Epaned may both be administered orally. Dose: Numerical similarity in dose (i.e. Emend 125 mg and Epaned 1.25 mg for a pediatric patient weighing 15.6 kg dosed at 0.08 mg/kg) Frequency: Both may be prescribed once daily.	Orthographic: The 'p' in Epaned and the 'm' in Emend at the 2nd position appear different. Epaned contains an extra vowel before the last letter 'd' whereas Emend does not. Strength: Emend is available in multiple strengths, therefore a prescriber would need to specify the strength. Epaned is available in one strength therefore the strength could be omitted

	via intravenous infusion on Day 1		
2.	Opana (Oxymorphone Hydrochloride) Tablet and Injection Strength: Tablet: 5 mg, 10 mg Injection: 1 mg/mL Dose: Tablet: 5 mg to 20 mg orally every 4 to 6 hours as needed; titrated to adequate pain relief Injection: Initially 0.5 mg to 1.5 mg subcutaneously or intramuscularly every 4 to 6 hours as needed; titrated to adequate pain relief	Orthographic: The name "opana" and the letter string "epane" in Epaned look similar when scripted. Phonetic: The 'o' sound in Opana and 'e' sound in Epaned are similar. Both contain similar syllables "pan" in Opana and "pan" in Epaned. Dose: Overlap in dose (i.e. 5 mg), although the safety and effectiveness of Opana in pediatrics (<18) has not been established. Route: Both may be administered orally Strength: Overlap in strength of 1 mg/mL	Orthographic: Epaned contains an extra letter 'd' at the end, making the name appear longer than Opana when scripted and imparting a visual difference due to the upstroke. Phonetic: The last syllable 'a' in Opana and 'ed' in Epaned sound different. Frequency: Opana is 4 to 6 hours as needed vs. Epaned is once daily
3.	Exparel (Bupivacaine) Liposomal Injection Strength: 13.3 mg/mL Dose: 106 mg (8 mL) or 266 mg (20 mL) injected into soft tissue	Orthographic: Both begin with 'E' and contain the letter 'p' in the prefix of the name followed by the letter 'a'. The 'r' in Exparel appears similar to 'n' in Epaned when scripted. The letter string 'el' appears similar to the letter 'd' when scripted. Dose: Numerical similarity in dose (i.e. Exparel 266 mg and Epaned 2.66 mg for a patient weighing 33.25 kg dosed at 0.08 mg/kg)	Orthographic: The letter string 'ne' in Epaned looks different from 'r' in Exparel when scripted. Frequency: Exparel is one time vs. Epaned is once daily.

4.	Eye-Sed (Zinc Sulfate) Ophthalmic Solution Strength: 0.25% Dose: 1 to 2 drops into affected eye up to 4 times daily	Orthographic: Both begin with 'E' followed by a down stroke. Both contain the letter string 'ed' in the suffix. Frequency: Orthographic similarity in qid and qd.	
5.	Apacet (Acetaminophen) Capsule, Tablet, Oral solution, Oral elixir Strength: Tablet: 325 mg, 500 mg Capsule: 500 mg Chewable Tablet: 80 mg Oral Solution: 80 mg/0.8 mL Oral Elixir: 160 mg/5 mL Dose: 325 mg to 650 mg every 4 to 6 hours as needed or 1000 mg 3 to 4 times daily as needed, maximum of 4 grams/day, or 10 to 15 mg/kg/dose every 4 to 6 hours as needed, not to exceed 5 doses in 24 hours.	Orthographic: Both begin with vowels that appear similar when scripted, followed by the letter string 'pa' at the 2nd and 3rd position. The letter string 'et' in Apacet appears similar to 'd' in Epaned when scripted. Dose: Numerical similarity in dose (i.e. Epaned 3.25 mg for a patient weighing 40.6 kg vs. Apacet 325 mg)	Orthographic: The letter string 'ne' in Epaned looks different from 'c' in Apacet when scripted. Frequency: Apacet is every 4 to 6 hours as needed vs. Epaned is once daily
6.	Agoral Maximum Strength Laxative Liquid (Sennocides A and B) Strength: 8.3 mg/5 mL	Orthographic: Both begin with a vowel 'a' and 'e' which look similar when scripted followed by a down stroke. The 'al' in Agoral looks similar to the 'd' in Epaned when scripted.	Orthographic: The letter string 'ne' in Epaned looks different from 'r' in Agoral when scripted. Dose: Numerical similarity in dose (i.e. Agoral 3 tsp and

	Dose: 3 to 6 teaspoons orally up to 2 times daily	Frequency: Both may be administered once daily since Agoral may be used up to twice daily.	Epaned 3 mL), although tsp and mL may help to differentiate.
7.	Epinal (Epinephrine Borate) ophthalmic solution Strength: 1%, 0.5% Dose: 1 drop into affected eye 1 to 2 times daily	Orthographic: Both begin with the letter 'E' and contain the letter 'p' at the 2nd position. Both contain 'n' at the 4th position. The letter string 'al' in Epinal looks similar to the letter 'd' in Epaned when scripted. Frequency: Both may be administered once daily	Orthographic: The letter string 'ne' in Epaned looks different from 'n' in Epinal when scripted. Strength: There is numerical similarity in strength (i.e. Epaned 1 mg/mL and Epinal 1%), although % and mg/mL would help to differentiate and help to prevent the failure. Dose: Numerical similarity in dose (i.e. Epinal 1 gtt and Epaned 1 tsp), although gtt and tsp may help to differentiate.
8.	Equanil (Meprobamate) Tablet and Capsule Strength: Tablet: 200 mg, 400 mg Capsule: 400 mg Dose: Adults: 1200 mg to 1600 mg orally daily in 3 or 4 divided doses; maximum 2400 mg per day. Children: 100 mg to 200 mg orally 2 to 3 times daily; maximum 600 mg per day Renal: Every 9 to 18 hours	Orthographic: Both begin with the letter 'E' and contain a down stroke at the 2nd position. The letter string 'il' in Equanil looks similar to 'd' when scripted. Frequency: Orthographic similarity in qid and qd.	Orthographic: The letter string 'an' in Equanil looks different from 'ne' in Epaned when scripted. Dose: Doses do not overlap. The dose of Equanil 100 mg is achievable with various doses of Epaned (i.e. 2 mg or 5 mg); however the dose of the Epaned would be outside of the normal dosing range.

	Brand is discontinued, but generics are available		
9.	Aquanil HC (Hydrocortisone) Lotion Strength: 1% Dose: Apply to affected area 2 to 4 times daily	Orthographic: Both begin with a vowel, followed by a down stroke which appears similar when scripted. The letter string 'il' in Aquanil looks similar to 'd' in Epaned when scripted. Frequency: Orthographic similarity in qid and qd.	Orthographic: The letter string 'an' in Aquanil looks different from 'ne' in Epaned when scripted. Dose: A dose for Epaned will need to be specified based on weight vs. no specific dose needs to be specified for Aquanil or the dose is expressed as a small or sufficient amount or thin layer.
10.	Epimide-50 (Urea) Topical Paste Strength: 50% Dose: Apply to the affected area twice daily	Orthographic: Both begin with 'Ep'. The 'm' in Epimide looks similar to 'n' in Epaned when scripted. Both contain a 'd' in the suffix.	Orthographic: There is an extra 'e' at the end of Epimide vs. no letter after 'd' in Epaned. Dose: A dose for Epaned will need to be specified based on weight vs. no specific dose needs to be specified for Epimide or the dose is expressed as a small or sufficient amount or thin layer.
11.	Epipen (Epinephrine) Injection Strength: USP 1:1000, 0.3 mL Dose: 0.3 mg intramuscularly or subcutaneously once	Orthographic: Both begin with 'Ep'. Phonetic: The 'epics' sound in Epipen and 'epa' sound in Epaned are similar. Dose: Numerical similarity in dose (i.e. Epipen .3 mg and 3 mg Epaned for a 37.5 kg patient)	Orthographic: The letter string 'pen' in Epipen looks different from letter string 'ned' in Epaned when scripted. Phonetic: The 'pen' in Epipen and 'ned' in Epaned sounds different. Route: Epipen is available in

			multiple routes therefore the route would need to be specified on a prescription vs. Epaned is only one route; therefore the route may be omitted. The routes do not overlap. Frequency: Epipen is one time vs. Epaned is once daily
12.	Episil (Ethanol, propylene glycol, soy lecithin) Liquid Dose: Apply 1 to 3 pumps to the oral cavity 2 to 3 times daily, or as needed	Orthographic: Both begin with 'Ep'. The letter string 'il' in Episil looks similar to the 'd' in Epaned when scripted.	Orthographic: The 's' in Episil and the letter string 'ne' in Epaned look different when scripted. Dose: Numerical overlap in dose (i.e. 3 pumps and 3 mL), although pumps and mL may help to differentiate.
13.	(b) (4)		

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	once daily NDA 203992 Application was voluntarily withdrawn (filed, but not approved) 3/20/2012		
14.	Apurol (Allopurinol) Tablet Strength: 100 mg, 300 mg Dose: 100 mg to 800 mg per day, administered orally once daily or in 2 to 3 divided doses if > 300 mg/day	Orthographic: Both begin with a vowel which appears similar when scripted, followed by 'p'. The letter 'r' in Apurol looks similar to the letter 'n' in Epaned when scripted. The letter string 'ol' looks similar to 'd' in Epaned when scripted. Frequency: Both can be administered once daily.	Orthographic: The 'r' in Apurol and letter string 'ne' in Epaned looks different when scripted. Dose: Dose does not overlap. The dose of Apurol 100 mg is achievable with various doses of Epaned (i.e. 2 mg, 5 mg); however the dose of the Epaned would be outside of the normal dosing range.
15.	Epivir (Lamivudine) Tablet and Oral Solution Strength: Tablet: 150 mg, 300 mg Oral solution: 10 mg/mL Dose: Adults: 150 mg orally twice daily, or 300 mg orally once daily Children: 4 mg/kg twice daily to a maximum of 150 mg twice daily, or: Pediatric dosing for Epivir tablets: 14 to 21 kg: 75 mg in AM and 75 mg in	Orthographic: Both begin with 'Ep'. The 'v' in Epivir looks similar to 'n' in Epaned when scripted. Dose: Numerical similarity in dose (i.e. Epivir 150 mg and Epaned 1.5 mg for a patient weighing 18.7 kg dosed at 0.08 mg/kg) Frequency: Both may be administered once daily.	Orthographic: The 'r' in Epivir and 'd' in Epaned looks different when scripted.

	PM >21 to < 30: 75 mg AM and 150 mg in PM >,= 30: 150 mg in AM and 150 mg in PM Renal adjustments in adults and adolescents (if CrCL): >=50: 150 mg twice daily or 300 mg once daily 30-49: 150 mg once daily 15-29: 150 mg first dose, then 100 mg once daily 5-14: 150 mg first dose, then 50 mg once daily <5: 50 mg first dose, then 25 mg once daily		
16.	Atamet (Carbidopa/Levodopa) Tablet Strength: 25 mg/100 mg; 25 mg/250 mg Dose: 1 to 2 tablets orally three to four times daily up to maximum of 8 tablets daily	Orthographic: Both begin with vowels which appear similar when scripted. The 'm' in Atamet looks similar to 'n' in Epaned when scripted. Both end with an upstroke. Phonetic: The first syllables 'a' in Atamet and 'e' in Epaned sound similar. The 3rd syllable 'met' in Atamet sounds similar to the 3rd syllable 'ned' in Epaned. Dose: Numerical overlap in dose (i.e. 1 tab and 1 tsp). There is also orthographic	Orthographic: The first 't' in Atamet is an upstroke vs. 'p' in Epaned is down stroke. The last 't' in Atamet is a cross stroke vs. the 'd' in Epaned is an upstroke only. Phonetic: The 2nd syllable 'ta' in Atamet sounds different from the 2nd syllable 'pa' in Epaned. Strength: Although there is similarity in the dose of 1 tab vs. 1 tsp, in order to order 1 tab of Atamet, you would have to specify the strength, whereas

		similarity in the unit of measure. Frequency: Orthographic similarity in qid and qd.	for Epaned the strength would not have to be specified. There is no overlap between the strengths of the two products, or the strengths of Atamet and the dosing of Epaned.
17.	Obenix (Phentermine hydrochloride) Capsule Strength: 37.5 mg Dose: 37.5 mg orally once daily, or 18.75 mg (1/2 tablet) orally once or twice daily Brand name product is discontinued, but generic is available	Phonetic: The first syllables 'obe' in Obenix and 'epa' in Epaned sound similar. Frequency: Both are administered once daily. Dose: Numerical overlap in dose (i.e. Obenix 37.5 mg and Epaned 3.75 mg for a patient weighing 46.87 kg)	Phonetic: The 3rd syllable 'nix' in Obenix and the 3rd syllable 'ned' in Epaned sounds different.
18.	Aquoral (Oxidized glycerol triesters and silicon dioxide) Oral Spray Strength: N/A Dose: 2 sprays 3 to 4 times daily	Orthographic: Both begin with a vowel, followed by a down stroke which appears similar when scripted. The letter string 'al' in Aquoral looks similar to 'd' in Epaned when scripted. Frequency: Orthographic similarity in qid and qd.	Orthographic: The letter string 'or' in Aquoral looks different from 'ne' in Epaned when scripted. Dose: Numerical similarity in dose (i.e. 2 sprays and 2 mg), although 'sprays' and 'mg' or 'mL' would help to differentiate.
19.	Eperbel-S (Belladonna Alkaloids, Ergotamine Tartrate, Phenobarbital) Tablet Strength: Belladonna Alkaloids 0.2 mg, Ergotamine	Orthographic: Both begin with 'Ep' followed by a vowel which looks similar when scripted. The letter string 'el' in Eperbel looks similar to the letter 'd' in Epaned when scripted.	Orthographic: Eperbel contains an upstroke in the infix vs. Epaned contains no upstroke in the infix.

	Tartrate 0.6 mg, Phenobarbital 40 mg Dose: 1 tablet orally twice daily	Dose: Numerical overlap in dose (i.e. 1 tab and 1 tsp). Tab and tsp are orthographically similar also.	
20.	Elavil (Amitriptyline hydrochloride) Injection and Tablet Strength: Tablet: 10 mg, 25 mg, 50 mg, 75 mg, 100 mg, 150 mg Injection: 10 mg/mL Dose: Tablet: 10 mg to 300 mg orally per day in divided doses (doses < 150 mg/day can be given as a single dose at bedtime) Injection: 20 mg to 30 mg intramuscularly three times daily	Orthographic: Both begin with 'E' with an 'a' at the 3rd position. The 'v' in Elavil looks similar to the 'n' in Epaned when scripted. The letter string 'il' in Elavil looks similar to 'd' in Epaned when scripted. Frequency: Both may be administered once daily. Dose: Numerical similarity in dose (i.e. Elavil 20 mg and Epaned 2 mg)	Orthographic: The 'l' in Elavil is an upstroke vs. 'p' in Epaned is a downstroke.
21.	Clomid (Clomiphene Citrate) Tablet Strength: 50 mg Dose: 50 mg orally once daily for 5 days. If no ovulation occurs, 100 mg orally once daily for 5 days	Orthographic: The 'c' in Clomid and 'e' in Epaned looks similar when scripted. The 'om' in Clomid looks similar to 'an' in Epaned. Both end with a 'd'. Dose: Numerical similarity in dose (i.e. Clomid 50 mg and Epaned 5 mg) Frequency: Both may be administered once daily.	Orthographic: The 'l' in Clomid looks different from 'p' in Epaned when scripted.
22.	Fluonid (Fluocinolone	Orthographic: The letter 'F' in Fluonid and	Orthographic: The letter string 'luo' in

	Acetonide) Cream, Gel, Ointment, Topical Solution Strength: Cream 0.025% Gel 0.025% Ointment 0.025% Topical Solution 0.01% Dose: Apply to affected area 2 to 4 times daily	'E' in Epaned look similar when scripted. Both contain an 'n' in the infix and ends with 'd'. Frequency: Orthographic similarity in qid and qd.	Fluonid looks different the letter string 'pa' in Epaned when scripted. Dosage form: Fluonid is available in multiple dosage forms; therefore the dosage form would need to be specified on a prescription. Epaned is only available in in a single dosage form; therefore, the dosage form may be omitted on a prescription. There are no overlaps in dosage form. Dose: A dose for Epaned will need to be specified based on weight vs. no specific dose needs to be specified for Fluonid or the dose is expressed as a small or sufficient amount or thin layer.
23.	Alomide (Lodoxamide Tromethamine) Ophthalmic Solution Strength: 0.1% Dose: 1 to 2 drops in each affected eye 4 times daily	Orthographic: Both begin with vowels which look similar when scripted. The 'om' in Alomide and 'an' in Epaned look similar when scripted. Both contain a 'd' in the suffix. Frequency: Orthographic similarity in qid and qd.	Orthographic: The 'l' in Alomide looks different from 'p' in Epaned. There is an extra 'e' after the 'd' in Alomide vs. none in Epaned. Dose: Numerical overlap in dose (i.e. 1 gtt and 1 tsp or 1 mg), although gtt and tsp or mg may help to differentiate.
24.	Abelcet (Amphotericin B) Injection Strength: 5 mg/mL Dose: 5 mg/kg/day as a	Phonetic: The first syllables 'abe' in Abelcet and 'epa' in Epaned sound similar. Dose: Numerical similarity in dose (i.e. Abelcet 500 mg for patient weighing 100 kg and	Phonetic: The 3rd syllable 'cet' in Abelcet and the 3rd syllable 'ned' in Epaned sounds different.

	single intravenous infusion or 5 mg/kg daily	Epaned 5 mg) Frequency: Both may be administered once daily.	
25.	Equi-cet (Acetaminophen/ Butalbital/ Caffeine) Tablet Strength: 325mg/50 mg/40 mg Dose: 1 to 2 tablets orally every 4 hours as needed, not to exceed 6 tablets in 24 hours	Orthographic: Both begin with 'E' followed by a down stroke. Both end with an upstroke. Dose: Numerical overlap in dose (i.e. 1 tab and 1 tsp). Tab and tsp are orthographically similar also.	Orthographic: The letter string 'ic' in Equi-cet if written without the '-' mark looks different from the letter 'n' in Epaned. Frequency: Equi-cet is every 4 hours as needed vs. Epaned is once daily.
26.	Epivar (2a,3a-epithio-17a-methyl-5a-androstan-17b-ol) Capsule Strength: 18 mg Dose: Take 2 to 3 capsules per day for a maximum of 5 weeks. Administer in 3 divided doses.	Orthographic: Both begin with 'Ep'. The 'v' in Epivar looks similar to the 'n' in Epaned when scripted. The 'a' in Epivar looks similar to 'e' in Epaned when scripted.	Orthographic: The 'r' in Epivar looks different from 'd' in Epaned when scripted. Frequency: Epivar is three times daily vs. Epaned is once daily. Dose: Numerical overlap in dose (i.e. Epivar 2 caps and Epaned 2 mg), although caps and mg may help to differentiate.
27.	Epovar Epovar Orovar-CC, Di-Arginine Orotate, Magnesium Orotate, Potassium Orotate Strength: Epovar Orovar-CC 3012 mg, Di-Arginine Orotate 1500 mg, Magnesium Orotate 1500 mg, Potassium	Orthographic: Both begin with 'Ep', followed by a vowel that looks similar when scripted. The 'v' in Epovar looks similar to the 'n' in Epaned when scripted. The 'a' in Epovar looks similar to 'e' in Epaned when scripted.	Orthographic: The 'r' in Epovar looks different from 'd' in Epaned when scripted. Frequency: Epovar is three times daily vs. Epaned is once daily. Dose: Numerical overlap in dose (i.e. Epovar 2 caps and Epaned 2 mg), although caps

	Orotate 12 mg Dose: As a dietary supplement take 2 to 3 caplets 3 times daily Training and Competition: Take 3 caplets 90 to 120 minutes before event.		and mg may help to differentiate.
28.	Epimax (2a,3a-epithio-17a-methyl-Sa-androstan-1 7b-ol) Capsule Strength: 18 mg Dose: 1 to 3 capsules daily.	Orthographic: Both begin with 'Ep'. The 'm' in Epimax and 'n' in Epaned look similar when scripted. Frequency: Both may be administered once daily.	Orthographic: The 'x' in Epimax looks different from the 'd' in Epaned. Dose: Numerical similarity in dose (i.e. Epimax 1 cap and Epaned 1 tsp), although cap and tsp may help to differentiate.
29.	Epinephrine or epineph **Dosage formulation and strengths:** Injection solution: 0.1 mg/mL (10 mL) [1:10,000]; 1 mg/mL (1 mL) [1:1000] Injection solution, as hydrochloride: 1 mg/mL (30 mL) [1:1000] Injection solution, as hydrochloride: 1 mg/mL (1 mL) [1:1000] Solution for oral inhalation: 2.25% (0.5 mL)	Orthographic: The 'epine' in epinephrine (or abbreviation, Epineph) and the 'epane' in Epaned look similar when scripted. Both Epaned and abbreviated form end with upstroke. Phonetic: The 'epineph' in Epinephrine and in the abbreviation, Epineph sounds similar to Epaned when spoken. Strength: Overlap in 1 mg/mL Dose: Numerical similarity in dose (i.e. epinephrine .3 mg and Epaned 3 mg, or epinephrine 3 mg dosed at 0.1 mg/kg for	Orthographic: The 'phrine' in epinephrine and 'd' in Epaned look different when scripted. The letter string 'ph' in Epineph (abbreviation for epinephrine per MediLexicon) looks different from 'd' in Epaned when scripted. Phonetic: The 'phrine' in epinephrine and 'd' in Epaned sound different. If a verbal order was given for the abbreviated 'epineph', the end of the third syllables sound different. Frequency: Epinephrine is one time or as needed at various intervals vs. Epaned is once

	Solution, intranasal as hydrochloride: 1 mg/mL (30 mL) [1:1000] Dose: **Asystole**: 1 mg (up to 0.2 mg/kg) intravenous (IV) or intraosseous (IO) every 3 to 5 minutes (0.01 mg/kg every 3 to 5 minutes for pediatric), or 2 to 2.5 mg endotracheal every 3 to 5 minutes until IV/IO access established (or 0.1 mg/kg every 3 to 5 minutes if pediatric) **Post resuscitation infusion:** 0.1 to 1 mcg/kg/minute IV or IO if pediatric **Bradycardia:** 0.1 to 0.5 mcg/kg/minute IV infusion titrated to desired effect (or 0.01 mg/kg IV/IO every 3 to 5 minutes as needed if pediatric), or 0.1 mg/kg endotracheal every 3 to 5 minutes as need if pediatric, or 0.1 to 1 mcg/kg/min via IV/IO infusion if pediatric **Bronchodilator:** *SQ (Subcutaneous)*: 0.3 to 0.5 mg every 20 minutes for 3	a 30 kg patient and Epaned 3 mg dosed at 0.08 mg/kg for a 37.5 kg patient)	daily Route/Formulation: Epinephrine may be administered by multiple routes and various formulations, therefore the route of administration and/or formulation is likely to be specified on a prescription vs. Epaned is available by one route and may be omitted. The routes do not overlap.

	doses (0.01 mg/kg every 20 minutes for 3 doses if pediatric) *Nebulization*: 1 to 3 inhalations up to every 3 hours if needed (hand bulb), or 0.5 mL to nebulizer and dilute with 3 mL of normal saline (NS) over 15 minutes every 3 to 4 hours as needed (0.05 mL/kg diluted in 3 mL of NS administered over 15 minutes no more frequently than every 2 hours if pediatric) *Inhalation*: 1 inhalation, may repeat once after 1 minute, but do not use again for at least 3 hours. **Hypersensitivity:** *IM (Intramuscular), SQ*: 0.2 to 0.5 mg every 5 to 15 minutes (0.01 mg/kg every 5 to 15 minutes if pediatric) *IV*: 0.1 mg over 5 minutes, may infuse at 1 to 15 mcg/min *IM, SQ*: 0.3 mg once, dose may be repeated (0.15 mg once, dose may be repeated if pediatric) **Mydriasis**: Use as need during procedure or may administer		

	intracamerally with a bolus dose of 0.1 mL of a 1:100,000 to 1:400000 dilution Intranasal: Apply solution locally as drops or spray or with sterile swab.		
30.	(b) (4) [redacted]		
31.	Enovid (Norethyndorel/	Orthographic: Both start with ‘e’. The	Orthographic: The ‘n’ in Enovid and ‘p’ in

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	Mestranol) Tablet Strength: 0.075 mg/5 mg 0.15 mg/9.85 mg Dose: 1 tablet orally once daily NDA 010976 Withdrawn FR effective 6/18/09. Product discontinued with no generics available.	letter string 'ovid' in Enovid and 'aned' in Epaned look similar. Dose: Numerical similarity in dose (i.e. Enovid 1 tab and Epaned 1 tsp). Tab and tsp are orthographically similar. Frequency: Both are once daily.	Epaned look different. Strength: Enovid is available in multiple strengths; therefore a prescriber would need to specify the strength. Epaned is available in one strength therefore the strength could be omitted.
32.	(b) (4)		

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/s/

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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:	February 17, 2013
Reviewer:	Kimberly DeFronzo, RPh, MS, MBA Division of Medication Error Prevention and Analysis
Team Leader:	Irene Z. Chan, PharmD, BCPS Division of Medication Error Prevention and Analysis
Drug Name and Strength(s):	(b) (4) (Enalapril Maleate) Powder for Oral Solution 1 mg/mL
Application Type/Number:	NDA 204308
Applicant/Sponsor:	Silvergate Pharmaceuticals
OSE RCM #:	2013-282

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1 INTRODUCTION

This review evaluates the proposed proprietary name (b) (4) (Enalapril Maleate) for NDA 204308. The proposed proprietary name was submitted by Silvergate Pharmaceuticals for evaluation on January 15, 2013.

1.1 REGULATORY HISTORY

DMEPA previously evaluated the proposed proprietary name (b) (4) for this NDA under OSE RCM #2012-1911. On October 17, 2012, DMEPA held a teleconference with the Applicant to inform the Applicant of our preliminary concerns with the proposed proprietary name, (b) (4), due to it containing a significant portion of the established name.

On October 23, 2012, the Applicant formally withdrew the Request for Proprietary Name Review of (b) (4)

1.2 PRODUCT INFORMATION

- Established Name: Enalapril Maleate
- Indication of Use: For the treatment of hypertension in pediatric patients (b) (4) of age
- Route of Administration: Oral
- Dosage Form: Powder for Oral Solution
- Strength: 1 mg/mL
- Dose and Frequency: The usual recommended starting dose is 0.08 mg/kg (up to 5 mg) once daily. Dosage should be adjusted according to blood pressure response.
- How Supplied: Powder for Oral Solution contains 150 mg of Enalapril Maleate powder in a 150-mL bottle. Reconstitution with 150 mL of the provided Ora-Sweet SF results in a 1 mg/mL oral solution. The product is supplied as a kit:
    - One 150 mL bottle contains 150 mg of Enalapril Maleate powder for oral solution in an HDPE bottle with child-resistant cap to provide 150 mg of Enalapril Maleate per bottle. NDC 52652-xxx-xx
    - One 150 mL bottle of Ora-Sweet SF (to be mixed with the powder)
- Storage: Store dry powder at controlled room temperature 15-30°C (59-86°F).
- Container and Closure systems: The primary container for the proposed drug product is a (b) (4) white HDPE bottle and a polypropylene child resistant cap with a heat induction foil inner seal.

2 DISCUSSION

During the initial steps of the proprietary name review process, the Office of Prescription Drug Promotion (OPDP) did not recommend the use of the proposed proprietary name

(b) (4) because it is overly fanciful and suggests that the drug has some unique effectiveness or composition attributable to the product. OPDP provided the following statement:

(b) (4)

This concern was shared with the Division of Cardiovascular and Renal Products (DCRP). In email correspondence dated February 12, 2013, DCRP concurred with OPDP's assessment. DMEPA also concurs with this finding and will not perform a safety assessment of the proposed proprietary name.

3 CONCLUSIONS AND RECOMMENDATIONS

The proposed proprietary name, (b) (4) is unacceptable from a promotional perspective. The Applicant will be notified of FDA's decision to object to the name based on promotional concerns via letter.

3.1 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, (b) (4) and have concluded that this name is unacceptable for the following reason:

(b) (4)

Please note that the Federal Food Drug and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made, whether through a proposed trade name or otherwise; this includes suggestions that a drug is better, more effective, useful in a broader range of conditions or patients, safer, has fewer, or lower incidence of, or less serious side effects or contraindications than has been demonstrated by substantial evidence or substantial clinical experience. [21 U.S.C. 321(n); see also 21 U.S.C. 352(a) & (n); 21 CFR 202.1(e)(5)(i);(e)(6)(i)].

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02/17/2013

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