

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**202342Orig1s000**

**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: November 7, 2011

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Drug Name(s): (b) (4) (Esomeprazole Strontium) Capsules

Strengths: 20 mg and 40 mg

Application Type/Number: NDA 202342

Applicant/sponsor: Parexel

OSE RCM #: 2011-3165

\*\*\* 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, (b) (4) 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 submitted the name (b) (4) which was found unacceptable by DMEPA in OSE review #2010-2275 due to orthographic and phonetic similarities to (b) (4). The Applicant subsequently withdrew the name and submitted a new proprietary name (b) (4) which was found unacceptable in OSE review # 2011-2255 due to phonetic similarities to Esomeprazole. The applicant subsequently withdrew the name and submitted a new proprietary name, (b) (4).

### 1.2 PRODUCT INFORMATION

(b) (4) (Esomeprazole Strontium) Delayed-release Capsules are indicated for the treatment of gastroesophageal reflux disease, risk reduction of NSAID-associated gastric ulcer, H. pylori eradication to reduce the risk of duodenal ulcer recurrence, and pathological hypersecretory conditions including Zollinger-Ellison syndrome. (b) (4) is recommended for use in adult patients. The recommended dose depends on the indication and varies from 20 mg or 40 mg by mouth once daily to 40 mg orally twice daily.

(b) (4) will be a prescription product available as a delayed release capsule in 20 mg and 40 mg strengths and supplied in bottles containing 30 capsules.

## 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 Gastroenterology/Inborn Error Products (DGIEP) and 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 evaluation.

#### 2.2.1 *United States Adopted Names (USAN) SEARCH*

The October 18, 2011 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 propose proprietary name is composed of a single word, (b) (4). Per the Applicant, the proprietary name has no intended meaning. The proposed name does not contain any

components (i.e. a modifier, route of administration, dosage form, etc.) that can contribute to medication error.

#### **2.2.4 FDA Name Simulation Studies**

Forty one practitioners participated in DMEPA's prescription studies. The most common misinterpretations in the written studies were 'a' and 'q' for 'o'. The most common misinterpretations in the voice study were adding the letter 's' or 'z' after the 'x' and 'u' for 'o'. (b) (4)

See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

#### **2.2.5 Comments from Other Review Disciplines**

In response to the OSE, May 5, 2011 e-mail, the Division of Gastroenterology/Inborn Error Products did not forward any comments or concerns relating to the proposed name at the initial phase of the name review.

#### **2.2.6 Failure Mode and Effects Analysis of Similar Names**

Appendix B lists possible orthographic and phonetic misinterpretations of the letters appearing in the propose name (b) (4) Table 1 on page 3 lists the names with orthographic, phonetic, or spelling similarity to the proposed proprietary name, (b) (4) identified by the primary reviewer, the Expert Panel Discussion (EPD), other review disciplines.

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

Look Similar		Sound Similar		Look and Sound Similar	
<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>
Exforge	EPD	Coprexa	EPD	Ixempra	EPD
Exefen	EPD	Encora	EPD	Exubera	EPD
Oxapro	EPD			Exparel	EPD
Clopra	EPD			Exalgo	EPD
Accupro	EPD				
Compro	EPD				
Exjade	EPD				
Axotal	EPD				
Evoxac	EPD				
Equetro	EPD				
Ertaczo	EPD				
Erypar	EPD				
Inspra	EPD				
Keppra	EPD				
Exna	EPD				
Lexapro	EPD				
Apidra	EPD				
Bextra	EPD				
Expain	EPD				
Enjuvia	SE				
Arixtra	SE				
(b) (4)	SE				
Extina	SE				
Esgic	SE				
(b) (4)	SE				

Our analysis of the thirty one names contained in Table 1 considered the information obtained in the previous sections along with their product characteristics. We determined that 29 of the 30 names will not pose a risk for confusion as described in Appendix D. However, (b) (4) has orthographic similarities, as well as overlapping product characteristics with (b) (4) that makes this name pair vulnerable to confusion in the usual practice setting as described in Section 3.1.1.

DMEPA communicated these findings to the DGEIP via e-mail on November 4, 2011. DGEIP provided no additional concerns with the proposed proprietary name (b) (4) in response to the DMEPA email.

### ***2.2.7 Confusion with Esomeprazole magnesium and Esomeprazole strontium***

The proposed product, Esomeprazole strontium, has an identical strength, dose, frequency, indication, and the same name, 'Esomeprazole' as compared to the currently marketed product Esomeprazole magnesium. However these products differ with respect the Pregnancy Category due to the unknown effects of the salt Strontium with regards to the fetus.

Due to the lack of safety data for the salt, strontium, in pregnant patients, Esomeprazole strontium will be given a Pregnancy Category C. This differs from the currently marketed Esomeprazole magnesium which is designated as a Pregnancy Category B. (b) (4)

(b) (4)

(b) (4)

### 3 CONCLUSIONS

DMEPA concludes the proposed proprietary name is acceptable from a promotional perspective but is not acceptable from a safety perspective. The proposed name is vulnerable to name confusion with (b) (4). Additionally, DMEPA has identified significant safety concerns (b) (4)

Therefore, the comments in Section 3.1 will be communicated to the Applicant via letter.

If you have further questions or need clarifications, please contact Nitin Patel, OSE Project Manager, at 301-796-5412.

#### 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 reasons provided in 3.1.1. DMEPA also identified significant safety concerns with the proposed product, Esomeprazole strontium, (b) (4)

Our concerns are highlighted in Section 3.1.2.

##### 3.1.1 (b) (4)

(b) (4)

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## 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.

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. ***Electronic online version of the FDA Orange Book***  
(<http://www.fda.gov/cder/ob/default.htm>)

The FDA Orange Book provides a compilation of approved drug products with therapeutic equivalence evaluations.

8. ***U.S. Patent and Trademark Office*** (<http://www.uspto.gov>)  
USPTO provides information regarding patent and trademarks.
9. ***Clinical Pharmacology Online*** ([www.clinicalpharmacology-ip.com](http://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.
10. ***Data provided by Thomson & Thomson's SAEGIS™ Online Service, available at*** ([www.thomson-thomson.com](http://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.
11. ***Natural Medicines Comprehensive Databases*** ([www.naturaldatabase.com](http://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.
12. ***Access Medicine*** ([www.accessmedicine.com](http://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.
13. ***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.
14. ***Red Book Pharmacy's Fundamental Reference***  
Red Book contains prices and product information for prescription, over-the-counter drugs, medical devices, and accessories.
15. ***Lexi-Comp*** ([www.lexi.com](http://www.lexi.com))  
Lexi-Comp is a web-based searchable version of the Drug Information Handbook.
16. ***Medical Abbreviations Book***  
Medical Abbreviations Book contains commonly used medical abbreviations and their definitions.

## 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.<sup>1</sup>

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

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<sup>1</sup> 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.<sup>2</sup> 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).

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<sup>2</sup> 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.

<b>Type of Similarity</b>	<b>Considerations when Searching the Databases</b>		
	<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"> <li>Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication</li> <li>Names may look similar when scripted and lead to drug name confusion in written communication</li> </ul>
	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"> <li>Names may look similar when scripted, and lead to drug name confusion in written communication</li> </ul>
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"> <li>Names may sound similar when pronounced and lead to drug name confusion in verbal communication</li> </ul>

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.<sup>3</sup> 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

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<sup>3</sup> 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, NAME	Scripted May Appear as	Spoken May Be Interpreted as
Capital ‘E’	I, F, L	“X”, “I”
lower case ‘x’	v, s	“ks”
lower case ‘o’	a, c u, or v	any vowel
lower case ‘p’	g, p, y, or z	“b”
lower case ‘r’	n, s, t, or v	
lower case ‘a’	o, e, u, c	Any vowel

**Appendix C: Prescription Simulation Samples and Results**

**Figure 1. Prescription Simulation Study (Conducted on August 26, 2011)**

<b>Handwritten Requisition Medication Order</b>	<b>Verbal Prescription</b>
<p><u>Medication Order:</u></p> <p>(b) (4) 40mg PO qdaily</p>	<p>(b) (4)</p> <p>40 mg</p> <p>po qdaily</p>
<p><u>Outpatient Prescription:</u></p> <p>(b) (4) 40mg</p> <p>it po daily</p>	

**FDA Prescription Simulation Responses.**

<b>Inpatient Medication Order</b>	<b>Outpatient Prescription</b>	<b>Voice Prescription</b>
(b) (4)		

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

<b>Proprietary Name</b>	<b>Active Ingredient</b>	<b>Similarity to Name of drug</b>	<b>Failure preventions</b>
(b) (4)			

**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.

<b>Proposed name:</b> <sup>(b) (4)</sup> (Esomeprazole Strontium) <b>Strength: 20 mg, 40 mg capsules</b> <b>Dose: One capsule (20 mg or 40 mg) by mouth once or twice daily</b>	<b>Causes of Failure Mode Resulting in Medication Error: Incorrect Product Ordered/ Selected/Dispensed or Administered Because of Name confusion</b>	<b>Prevention of Failure Mode: Orthographic/Phonetic/Product Characteristic Differences</b>
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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**

Date: January 6, 2011

Application Type/Number: NDA 202342

Through: Melina Griffis, RPh., Team Leader  
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From: Anne Crandall, Pharm.D., Safety Evaluator  
Division of Medication Error Prevention and Analysis

Subject: Proprietary Name Review

Drug Name(s): (b) (4) (Esomeprazole Strontium) Capsule, 20 mg and 40 mg

Applicant: Hanmi Pharmaceuticals

OSE RCM #: 2010-2275

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## EXECUTIVE SUMMARY

This review summarizes the Division of Medication Error Prevention and Analysis (DMEPA) proprietary name risk assessment for (b) (4) (Esomeprazole Strontium) Capsules (NDA 202342). Our evaluation finds the proposed name, (b) (4) vulnerable to name confusion with the proprietary name (b) (4) because of the orthographic and phonetic similarities, in addition to the overlapping product characteristics shared by this name pair. In addition, (b) (4) (b) (4) overlap with the established name Esomeprazole, which could contribute to confusion between these two names. Thus, we object to the use of the proposed proprietary name, (b) (4) for the product and provide comments under Section 4.2 explaining our analysis. The Applicant will be notified of these findings via letter.

## 1 BACKGROUND

### 1.1 INTRODUCTION

This review responds to a request from Parexel (on behalf of Hanmi Pharmaceuticals) dated October 19, 2010 for an assessment of the proposed proprietary name, (b) (4) regarding potential name confusion with other proprietary or established drug names in the usual practice setting. The Applicant also submitted container labels and labeling which will be evaluated separately in OSE review # 2010-2745.

### 1.2 PRODUCT INFORMATION

(b) (4) (Esomeprazole Strontium) Delayed-release Capsules are indicated for the treatment of gastroesophageal reflux disease, risk reduction of NSAID-associated gastric ulcer, H. pylori eradication to reduce the risk of duodenal ulcer recurrence, and pathological hypersecretory conditions including Zollinger-Ellison syndrome. (b) (4) is recommended for use in adult patients. The recommended dose depends on the indication and varies from 20 mg or 40 mg by mouth once daily to 40 mg orally twice daily.

(b) (4) will be a prescription product available as a delayed release capsule in 20 mg and 40 mg strength delayed release capsule and supplied in bottles containing 30 capsules.

## 2 METHODS AND MATERIALS

Appendix A describes the general methods and materials used by the Division of Medication Error Prevention and Analysis (DMEPA) when conducting a proprietary name risk assessment for all proprietary names. Sections 2.1, 2.2 and, 2.3 identify specific information associated with the methodology for reviewing the proposed proprietary name, (b) (4)

### 2.1 SEARCH CRITERIA

For this review, particular consideration was given to drug names beginning with the letter 'E' when searching to identify potentially similar drug names, as 75% of the confused drug names reported by the USP-ISMP Medication Error Reporting Program involve pairs beginning with the same letter.<sup>1,2</sup>

To identify drug names that may look similar to (b) (4) the DMEPA safety evaluators also consider the orthographic appearance of the name on the lined and unlined orders. Specific attributes taken into consideration include the (b) (4)

Additionally, several letters in the proposed name (b) (4) may be

<sup>1</sup> Institute for Safe Medication Practices. Confused Drug name List (1996-2006). Available at <http://www.ismp.org/Tools/confuseddrugnames.pdf>

<sup>2</sup> Kondrack, G and Dorr, B. Automatic Identification of Confusable Drug Names. Artificial Intelligence in Medicine (2005)

vulnerable to ambiguity when scripted (See Appendix B). As such, the DMEPA staff also considers these alternate appearances when identifying drug names that may look similar to

(b) (4)

When searching to identify potential names that may sound similar to (b) (4) the DMEPA staff searches for names with similar number of syllables (b) (4) and placement of vowel and consonant sounds. Additionally, DMEPA staff considers that pronunciation of part of the name can vary (Appendix B). The Applicant's intended pronunciation (b) (4) was also taken into consideration, as it was included in the Proprietary Name Review Request. Moreover, names are often mispronounced or spoken with regional accents and dialects, so other pronunciations of the names are considered.

## 2.2 FDA PRESCRIPTION ANALYSIS STUDIES

In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, the following inpatient and verbal orders were communicated during FDA prescription studies conducted on November 16, 2010.

## 3 RESULTS

### 3.1 DATABASE AND INFORMATION SOURCES

The DMEPA safety evaluators searches yielded a total of nineteen names (n=19) as having some similarity to the name (b) (4)

Thirteen (n=13) of the 19 names were thought to look like (b) (4). These names include (b) (4)

The remaining six (n=6) of the 19 names were thought to look and sound like (b) (4). These names included (b) (4)

Additionally, DMEPA's safety evaluators did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name as of November 1, 2010.

### 3.2 EXPERT PANEL DISCUSSION

The Expert Panel reviewed the pool of names identified by DMEPA staff (see Section 3.1 above) and noted no additional names thought to have orthographic or phonetic similarity to (b) (4)

DDMAC had no concerns regarding the proposed name from a promotional perspective, and did not offer any additional comments relating to the proposed name.

### 3.3 FDA PRESCRIPTION STUDIES ANALYSIS

A total of thirty practitioners responded to the prescription analysis studies. None of the responses overlapped with other drug names. Twenty one respondents interpreted the proposed name correctly as (b) (4) with correct interpretation occurring with inpatient orders (n=14), outpatient orders (n=6), and voice prescription studies (n=1). The most common misinterpretation of the remaining 9 prescriptions occurred with misinterpreting the first letter (b) (4)

(b) (4) See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

### 3.4 COMMENTS FROM THE DIVISION OF GASTROENTEROLOGY DRUG PRODUCTS

#### 3.4.1 Initial Phase of Review

In response to OSE email on December 8, 2010, the Division of Gastroenterology Products (DGP) forwarded no comments or concerns regarding the proposed proprietary name, (b) (4) at the initial point of review.

### 3.4.2 Midpoint of Review

DMEPA notified DGP via email on December 22, 2010 that we objected to the proposed proprietary name (b) (4). Per email correspondence from OGD on December 22, 2010 they indicated they concur with our assessment of the proposed proprietary name, (b) (4).

### 3.5 SAFETY EVALUATOR RISK ASSESSMENT OF PROPOSED PROPRIETARY NAME

The primary Safety Evaluator identified five (n=5) additional names, which were thought to look similar to (b) (4) and represent a potential source of drug name confusion. These names are (b) (4). Thus, total of 24 names were evaluated for the potential similarity to the proposed name (b) (4).

## 4 DISCUSSION

This proposed name, (b) (4) was evaluated from a safety and promotional perspective based on the product characteristics provided by the Applicant.

### 4.1 PROMOTIONAL ASSESSMENT

DDMAC did not find the name, (b) (4) promotional. DMEPA and DGP concurred with this finding.

### 4.2 SAFETY ASSESSMENT

DMEPA identified 24 names for their potential similarity to the proposed name (b) (4). No other aspects of the name were determined to be a potential source of confusion. Evaluation of the 24 names determined seven (n=7) could be eliminated for the reasons designated in Appendix E.

Failure Mode and Effect Analysis (FMEA) was then applied to determine if the proposed proprietary name could potentially be confused with the remaining 17 names and, thereby, lead to medication errors. This analysis determined that the name similarity between (b) (4) and 16 of the identified names was unlikely to result in medication error for the reasons provided in Appendix F.

However, our analysis of the remaining name, (b) (4) determined confusion was likely to result in medication errors between the proposed proprietary name, (b) (4) and the currently marketed product (b) (4). Our analysis is discussed below (Section 4.2.1 and 4.2.2).

#### 4.2.1 Sound-alike and Look-alike Similarity of (b) (4) and (b) (4)

The proposed proprietary name (b) (4) is orthographically and phonetically similar to (b) (4) and shares overlapping product characteristics that increase the risk of confusion. Although (b) (4)

(b) (4)

(b) (4)

(b) (4) and (b) (4) also share phonetic similarities that increase the risk of confusion. The phonetic similarities between (b) (4) and (b) (4) include: (b) (4)

(b) (4)

In addition to the orthographic and phonetic similarities, (b) (4) and (b) (4) share product characteristics and similar settings of use that increase the likelihood of a medication error to occur when used in the usual practice setting. These characteristics include dose (40 mg), route of administration (both only have one available route, therefore route may be excluded on order), frequency of administration (once or once daily), setting of use (hospital, especially intensive care area), and patient population (general use).

#### 4.2.2 (b) (4) and Esomeprazole

The first five letters in the proprietary name (b) (4) are derived from the established name Esomeprazole (Esome). The practice of deriving proprietary names from the established name defeats the intent of the proprietary name which is to serve as a unique identifier for the product. DMEPA discourages the use of proprietary names that look or sound-alike to their established name because it can increase the chance of confusion between the branded and established products which may not always be interchangeable due to different release mechanisms.

## 5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment determined the name is acceptable from a promotional perspective, however, (b) (4) is vulnerable to name confusion that could lead to medication errors with the currently marketed product, (b) (4). Thus, the Division of Medication Error Prevention and Analysis objects to the proprietary name, (b) (4) for this product. No alternative name was submitted for this NDA. Thus we will request the Applicant to submit an alternative name in our letter.

### 5.1 COMMENTS TO THE APPLICANT

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

The proposed proprietary name (b) (4) is orthographically and phonetically similar to (b) (4) and shares overlapping product characteristics that increase the risk of confusion. Although (b) (4)

(b) (4) In addition, both names are similar in length and shape and appear similar when scripted (see below).

(b) (4)

(b) (4) and (b) (4) also share phonetic similarities that increase the risk of confusion. The phonetic similarities between (b) (4) and (b) (4) include: (b) (4)

(b) (4)

significant portion of the established name defeats the intent of the proprietary name which is to serve as a unique identifier for the product.

## 6 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.

4. ***The Document Archiving, Reporting, and Regulatory Tracking System (DARRTS)***

DARRTS is a government database used to track individual submissions and assignments in 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. ***Electronic online version of the FDA Orange Book***  
(<http://www.fda.gov/cder/ob/default.htm>)

The FDA Orange Book provides a compilation of approved drug products with therapeutic equivalence evaluations.

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

USPTO provides information regarding patent and trademarks.

9. ***Clinical Pharmacology Online*** ([www.clinicalpharmacology-ip.com](http://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.

**10. Data provided by Thomson & Thomson's SAEGIS™ Online Service, available at ([www.thomson-thomson.com](http://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.

**11. Natural Medicines Comprehensive Databases ([www.naturaldatabase.com](http://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.

**12. Stat!Ref ([www.statref.com](http://www.statref.com))**

Stat!Ref contains full-text information from approximately 30 texts; it includes tables and references. Among the database titles are: Handbook of Adverse Drug Interactions, Rudolphs Pediatrics, Basic Clinical Pharmacology, and Dictionary of Medical Acronyms Abbreviations.

**13. USAN Stems (<http://www.ama-assn.org/ama/pub/category/4782.html>)**

USAN Stems List contains all the recognized USAN stems.

**14. Red Book Pharmacy's Fundamental Reference**

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

**15. Lexi-Comp ([www.lexi.com](http://www.lexi.com))**

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

**16. Medical Abbreviations Book**

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

## APPENDICES

### Appendix A:

FDA's Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name and the proprietary and established names of drug products existing in the marketplace and those pending IND, NDA, BLA, and ANDA products currently under review by the Center. 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.<sup>3</sup>

For the proposed proprietary name, DMEPA staff search a standard set of databases and information sources to identify names with orthographic and phonetic similarity and hold a Center for Drug Evaluation and Research (CDER) Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name. DMEPA staff also conducts internal CDER prescription analysis studies. When provided, DMEPA considers external prescription analysis study results and incorporate into the overall risk assessment.

The Safety Evaluator assigned to the Proprietary Name Risk Assessment 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 focuses on the avoidance of medication errors.

FMEA is a systematic tool for evaluating a process and identifying where and how it might fail.<sup>4</sup> DMEPA uses FMEA to analyze whether the drug names identified with orthographic or phonetic similarity to the proposed proprietary name could cause confusion that subsequently leads to medication errors in the clinical setting. 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.

In addition, the product characteristics provide the context for the verbal and written communication of the drug names and can interact with the orthographic and phonetic attributes of the names to increase the risk of confusion when there is overlap or, in some instances, decrease the risk of confusion by helping to differentiate the products through dissimilarity. Accordingly, the DMEPA staff considers the product characteristics associated with the proposed drug 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.

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. Because drug name confusion can occur at any point in the medication use process, DMEPA staff 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.<sup>5</sup> DMEPA provides the product characteristics considered for this review in section one.

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<sup>3</sup> National Coordinating Council for Medication Error Reporting and Prevention. <http://www.nccmerp.org/aboutMedErrors.html>. Last accessed 10/11/2007.

<sup>4</sup> Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

<sup>5</sup> Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006.

The Division of Medication Error Prevention and Analysis considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA also compares the spelling of the proposed proprietary name with the proprietary and established name of existing and proposed drug products because similarly spelled names may have greater likelihood to sound similar to one another when spoken or look similar to one another when scripted. DMEPA staff also examines the orthographic appearance of the proposed name using a number of different handwriting samples. Handwritten communication of drug names has a long-standing association with drug name confusion. Handwriting can cause similarly and even dissimilarly spelled drug name pairs to appear very similar to one another. The similar appearance of drug names when scripted has led to medication errors. The DMEPA staff applies expertise gained from root-cause analysis of such medication errors to identify sources of ambiguity within the name that could be introduced when scripting (e.g., “T” may look like “F,” lower case ‘a’ looks like a lower case ‘u,’ etc). Additionally, other orthographic attributes that determine the overall appearance of the drug name when scripted (see Table 1 below for details). In addition, the DMEPA staff 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. 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.

**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	<ul style="list-style-type: none"> <li>Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication</li> <li>Names may look similar when scripted and lead to drug name confusion in written communication</li> </ul>
	Orthographic similarity	Similar spelling Length of the name Upstrokes Down strokes Cross-strokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	<ul style="list-style-type: none"> <li>Names may look similar when scripted, and lead to drug name confusion in written communication</li> </ul>
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"> <li>Names may sound similar when pronounced and lead to drug name confusion in verbal communication</li> </ul>

Lastly, the DMEPA staff also 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 staff conducts searches of 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 using the criteria outlined in Section 2.1. Section 6 provides a standard description of the databases used in the searches. To complement the process, the DMEPA staff use 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, the DMEPA staff review 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.

## **2. CDER Expert Panel Discussion**

DMEPA conducts an Expert Panel Discussion to gather CDER professional opinions on the safety of the proposed product and the proposed proprietary name. The Expert Panel is composed of Division of Medication Errors Prevention (DMEPA) staff and representatives from the Division of Drug Marketing, Advertising, and Communications (DDMAC). 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 DMEPA staff to the Expert Panel for consideration. Based on the clinical and professional experiences of the Expert Panel members, the Panel may recommend the addition of 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 Analysis 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 the 123 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 send their interpretations of the orders via e-mail to DMEPA.

#### 4. Comments from the OND review Division or Generic drugs

DMEPA requests the Office of New Drugs (OND) or Office of Generic Drugs (OGD) Regulatory Division responsible for the application for their comments or concerns with the proposed proprietary name and 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 DDMAC's decision on the name. The primary Safety Evaluator addresses any comments or concerns in the safety evaluator's assessment.

The OND or 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 concur/not concur with DMEPA's final decision.

#### 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, conducts a Failure Mode and Effects Analysis, and provides an overall 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.<sup>6</sup> 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 characteristics listed in Section one. 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?”***

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. 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?”***

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<sup>6</sup> Institute for Healthcare Improvement (IHI). Failure Mode and Effects Analysis. Boston. IHI:2004.

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.

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 Risk Assessment:

- a. DDMAC finds the proposed proprietary name misleading from a promotional perspective, and the Review Division concurs with DDMAC'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.

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 is likely to recommend that the Sponsor select an alternative proprietary name and submit the alternate name to the Agency for DMEPA to 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 Sponsor. However, the safety concerns set forth in criteria a through e 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 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 a 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. . (See Section 4 for limitations of the process).

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 is likely to recommend that the Sponsor select an alternative proprietary name and submit the alternate name to the Agency for DMEPA to 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.

**Appendix B: Letters with possible orthographic or phonetic misinterpretation**

(b) (4)



**Appendix C: FDA Prescription study for  from 11/16/2010**

(b) (4)



**Appendix D:** Responses to prescription study 1116

<b>Inpatient Medication Order</b>	<b>Outpatient Prescription Order</b>	<b>Voice Prescription</b>
(b) (4)		

**Appendix E:** Drugs names which did not undergo FMEA analysis

<b>Drug Product Name</b>	<b>Reason for removal</b>
(b) (4)	

**Appendix F: Products with Differentiating Orthographic, Phonetic or Product Characteristics**

Product name with potential for confusion	Similarity to (b) (4)	Dosage form/ Strength	Usual Dose	Other Differentiating Product Characteristics
(b) (4) (Esomeprazole strontium)	N/A	20 mg, 40 mg oral capsule	Take 1 capsule by mouth once daily	

(b) (4)

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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ANNE CRANDALL  
01/06/2011

MELINA N GRIFFIS  
01/06/2011

CAROL A HOLQUIST  
01/07/2011