

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

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21-359

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 Medication Error Prevention and Risk Management**

Proprietary Name Review

Date: June 14, 2011
Application Type/Number: NDA 021359
Reviewer(s): Manizheh Siahpoushan, Pharm.D., Safety Evaluator
Division of Medication Error Prevention and Analysis
Team Leader Zachary Oleszczuk, Pharm.D., Team Leader
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Division Director Carol Holquist, RPh, Division Director
Division of Medication Error Prevention and Analysis
Drug Name(s): Rectiv (Nitroglycerin) Ointment, 0.4%
Applicant/sponsor: ProStrakan, Inc.
OSE RCM #: 2011-1658

*** 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, Rectiv, 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. The proposed product characteristics are provided in Appendix B.

1.1 REGULATORY HISTORY

Rectiv (Nitroglycerin) Ointment, 0.4% is the subject of a 505 (b) application, NDA 021359, submitted to the FDA on March 22, 2011. The name Rectiv, is the fourth proposed name for this product, submitted by the Applicant on May 26, 2011.

The first proposed proprietary name, Cellegesic, was found unacceptable by DMEPA in OSE Review #2009-1999, dated December 29, 2009 because of orthographic and phonetic similarities between Cellegesic and the marketed products, Calagesic and Alagesic. The second proposed proprietary name, Rectogesic was found unacceptable in OSE Review #2010-278, dated April 15, 2010, due to vulnerability to name confusion with the marketed Rectagene, Relagesic, and Rectacaine.

The third proposed proprietary name, (b)(4) was found unacceptable due to vulnerability to name confusion with the marketed proprietary names, Aviane and Altavera, based on orthographic similarities and shared product characteristics, and communicated to the Applicant, during a teleconference on May 2, 2011. DMEPA also found the alternate name, (b)(4) unacceptable due to vulnerability to name confusion with the marketed Neutrogena, based on orthographic similarities and shared product characteristics. DMEPA also communicated this with the Applicant during the teleconference on May 2, 2011.

2 RESULTS

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

2.1 PROMOTIONAL ASSESSMENT

DDMAC determined the proposed name is acceptable from a promotional perspective. The Division of Anesthesia and Analgesia Products (DAAP) and DMEPA concurred with the findings of DDMAC's promotional assessment of the proposed name.

2.2 SAFETY ASSESSMENT

The following information is considered in the safety assessment of the proposed name.

2.2.1 United States Adopted Names (USAN) SEARCH

The United States Adopted Name (USAN) stem search conducted on May 19, 2011, identified that a USAN stem is not present in the proposed proprietary name.

2.2.2 Components of the Proposed Proprietary Name that may contribute to errors

Review of the proposed name, noted that the name contained the letters, 'iv' which is an abbreviation for intravenous, a route of administration. Because this product is a topical ointment, inclusion of a different route of administration in the proposed name may be misleading and suggest the product may be for intravenous administration rather than topical administration.

There are five currently approved products that contain the letters 'iv' at the end of the proprietary name: Intuniv, Vibativ, Vpriv, Nexium IV, and Protonix IV. Four of these products require intravenous administration and only one product, Intuniv, requires oral administration only. An AERS database search performed by the primary safety evaluator on May 26, 2011, did not retrieve any reports of wrong route of administration errors for Intuniv.

For the proposed name, Rectiv, the letters 'iv' appear as prominent as the other letters in the name. The letters 'iv' are not separated from the name, capitalized, or bolded, to make the letters 'iv' more prominent in the name. Although, inclusion of the medical abbreviation 'iv' may be a possible source of confusion, the lack of prominence of this abbreviation, the lack of wrong route of administration error reports for Intuniv, and the fact that Rectiv is only available in a topical ointment, make it unlikely that the appearance of the letters 'iv' at the end of the proposed proprietary name, Rectiv, can lead to confusion with this product.

2.2.3 FDA Name Simulation Studies

Thirty-six practitioners responded to DMEPA's prescription studies. See Appendix D for the sample prescriptions used in the study and the complete listing of interpretations from the verbal and written prescription studies. None of responses overlapped with other drug names. Thirty-one participants interpreted the proposed proprietary name correctly as 'Rectiv' with eleven correct interpretations (n=11) occurring with inpatient orders, thirteen correct interpretation (n=13) occurring with outpatient orders, and seven correct interpretation (n=7) occurring with voice order. The remaining five participants misinterpreted the name, Rectiv. The most common misinterpretation occurred with four voice order participants adding an extra letter 'e' to the end of the name Rectiv (i.e. Rective) and one inpatient order participant misinterpreting the letter string '-ec-' as the letter 'u'. None of these misinterpretations caused any additional concerns that were not identified by DMEPA.

2.2.4 Comments from Other Review Disciplines

In response to the OSE e-mail, dated May 24, 2011, the Division of Anesthesia and Analgesia Products (DAAP) expressed concern that the name Rectiv may imply "correction or "corrective", but deferred to DMEPA for any promotional implications. The Division's comment was forwarded to DDMAC on May 26, 2011. DDMAC stated that although they considered the term 'corrective' in their original name evaluation, they did not however, feel that it was a strong objection. Therefore, DDMAC maintains its position regarding the proposed proprietary name, Rectiv. DMEPA concurred with DDMAC's assessment of the proposed name, and did not find the name Rectiv

promotional. The Division did not have any other comments or concerns relating to the proposed name at the initial phase of the name review.

2.2.5 Failure Mode and Effects Analysis of Similar Names

Table 1 lists the names found to have orthographic, phonetic, or spelling similarity to the proposed proprietary name, Rectiv. These names were identified by the primary reviewer and the Expert Panel (EPD).

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

Look Similar		Look and Sound Similar	
<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>
Rutin	EPD Panel	Factive	EPD Panel
Relera	EPD Panel	Vectical	EPD Panel
Reluri	EPD Panel	Vectibix	EPD Panel
Rectorex	EPD Panel		
Proactiv	EPD Panel		
Veltin	EPD Panel		
Rebif	EPD Panel		
Restasis	EPD Panel		
Revatio	EPD Panel		
Prefrin	EPD Panel		
Primlev	EPD Panel		
Rectasol HC	EPD Panel		
Retin A	EPD Panel		
Vantos	EPD Panel		
Videx	EPD Panel		
Rela	EPD Panel		
Reclast	EPD Panel		
Recort	EPD Panel		
RectaGel	EPD Panel		
Rectacaine	EPD Panel		
Relpax	EPD Panel		
Relistor	EPD Panel		

Relafen	EPD Panel		
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Our analysis of the 26 names contained in Table 1 considered the information obtained in the previous sections along with their product characteristics. We determined all 26 names will not pose a risk for confusion as described in Appendices E, F, and G.

DMEPA communicated these findings to the Division of Anesthesia and Analgesia via e-mail on May 31, 2011. At that time we requested additional information or concerns that could inform our review. The Division did not forward any additional concerns with the proposed proprietary name, Rectiv in response to our email.

3 CONCLUSIONS

DMEPA concludes the proposed proprietary name is acceptable from both a promotional and safety perspective. However, if any of the proposed product characteristics as stated in this review are altered, DMEPA rescinds this finding and the name must be resubmitted for review. The conclusions upon re-review are subject to change.

The proposed proprietary name, Rectiv, must be re-reviewed if the NDA approval is delayed beyond 90 days from the signature date of this review.

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)

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)

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)

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 Database* (<http://www.accessmedicine.com/drugs.aspx>)

Access Medicine contains full-text information from approximately 60 medical titles: it includes tables and references. Among the database titles are: Goodman and Gilman's The Pharmacological Basis of Therapeutics, Current Medical Diagnosis and Treatment, Tintinalli's Emergency Medicine, and Hurst's the Heart.

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)

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.

17. *LabelDataPlus Database* (<http://www.labeldataplus.com/index.php?ns=1>)

LabelDataPlus database covers a total of 36773 drug labels. This includes Human prescription drug labels as well as Active Pharmaceutical Ingredients (APIs), OTC (Application and Monograph) drugs, Homeopathic drugs, Unapproved drugs, and Veterinary drugs.

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.¹

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.² 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

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

² Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

monitoring the impact of the medication.³ DMEPA provides the product characteristics considered for this review in section one.

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		
	<i>Potential causes of drug name similarity</i>	<i>Attributes examined to identify similar drug names</i>	<i>Potential Effects</i>
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	<ul style="list-style-type: none"> Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication Names may look similar when scripted and lead to drug name confusion in written communication

³ Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006.

	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"> Names may look similar when scripted, and lead to drug name confusion in written communication
Sound-alike	Phonetic similarity	Identical prefix Identical infix Identical suffix Number of syllables Stresses Placement of vowel sounds Placement of consonant sounds Overlapping product characteristics	<ul style="list-style-type: none"> Names may sound similar when pronounced and lead to drug name confusion in verbal communication

Lastly, 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.⁴ 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

⁴ Institute for Healthcare Improvement (IHI). Failure Mode and Effects Analysis. Boston. IHI:2004.

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?”

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: Product Characteristics Provided for Rectiv

Rectiv
(Nitroglycerin) Ointment 0.4%

Indication: A nitrate vasodilator for treatment of moderate to severe pain associated with chronic anal fissure.

Route: Rectal

Dosage Form: Topical Ointment

Strengths: 0.4%

Dosage/Administration: 375 mg dose of ointment (1 inch), equivalent to 1.5 mg of Nitroglycerin is applied rectally approximately every 12 hours. Treatment should continue for up to 3 weeks.

How Supplied: 30 gram tube

Applicant: ProStrakan Inc.

Appendix C: Letters with possible orthographic or phonetic misinterpretation

Letters	Scripted may appear as	Spoken may be interpreted as
Capital 'R'	'B', 'Pr', 'K'	'WR'
Lower case 'e'	'a', 'i', 'l', 'p'	Any Vowel
Lower case 'c'	'a', 'e', 'i', 'l'	'z', 'k', 's' if followed by an e or i
Lower case 't'	'A', 'f', 'l'	'd'
Lower case 'i'	'e'	
Lower case 'v'	'r', 'u'	'f'

Appendix E: Names eliminated from further evaluation for reasons listed below

	Proprietary Name	Similarity to Rectiv	Reason Eliminated
1	Vantos	Look alike	Found only in the Access Medicine database with no other information or product characteristics available in any other databases.
2	Prefrin	Look alike	International brand name for phenylephrine ophthalmic.

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

	PROPOSED NAME: Rectiv (Nitroglycerin) Ointment	STRENGTH: 0.4%	USUAL DOSE: Apply 1 inch ointment rectally every 12 hours up to 3 weeks.
	FAILURE MODE: Name Confusion	CAUSES: (Potential reasons for name confusion that could lead to medication error)	PREVENTION OF FAILURE MODE (Reasons why the risk of medication error is minimized)
1	Rutin (Supplement found in buckwheat seed and fruits) Tablet, 500 mg <u>Usual Dose</u> One tablet daily as supplement.	<u>Orthographic</u> All letters in the name Rectiv may appear similar to all letters in Rutin when scripted <u>Strength</u> Single strength <u>Numerical Overlap in the Usual Dose</u> One inch vs. one tablet	<u>Dosage Form</u> Ointment vs. tablet <u>Route of Administration</u> Topical vs. oral <u>Frequency of Administration</u> Every 12 hours vs. once daily Additionally, a search of the use date indicated that Rutin was not prescribed in the last 8 years by healthcare practitioners and therefore there is less chance of medication errors that can result from orthographic similarities of the two names in the usual practice setting.

2	<p>Relera (Chlorpheniramine Maleate, Phenylephrine Hydrochloride) Caplet, 8 mg-20 mg (Discontinued, but generic equivalents are available)</p> <p><u>Usual Dose</u> Take 2 caplets orally every 12 hours.</p>	<p><u>Orthographic</u> Both names consist of six letters, 2 upstrokes ('R', 't' in Rectiv and 'R', 'l' in Relera) and start with the letter string 'Re-'. Additionally, the letter string '-iv-' in Rectiv may appear similar to the letter string '-er-' in Relera when scripted.</p> <p><u>Strength</u> Single strength</p> <p><u>Frequency of Administration</u> Every 12 hours</p>	<p><u>Dosage Form</u> Ointment vs. caplet</p> <p><u>Route of Administration</u> Topical vs. oral</p> <p><u>Usual Dose</u> 1 inch vs. 2 caplets</p>
3	<p>Factive (Gemifloxacin) Tablet, 320 mg</p> <p><u>Usual Dose</u> Take one tablet orally for 5 or 7 days.</p>	<p><u>Orthographic</u> The letter string '-ectiv' in Rectiv may appear similar to the letter string '-activ-' in Factive when scripted. Additionally, both names share the upstroke 't' in the same position.</p> <p><u>Strength</u> Single strength</p> <p><u>Numerical Overlap in the Usual Dose</u> 1 inch vs. 1 tablet</p>	<p><u>Orthographic</u> The name Factive appears longer than Rectiv when scripted because of an extra letter present in Factive. Additionally, the first letter 'R' in Rectiv does not appear similar to the first letter 'F' in factive when scripted.</p> <p><u>Dosage Form</u> Ointment vs. tablet</p> <p><u>Route of Administration</u> Topical vs. oral</p> <p><u>Frequency of Administration</u> Every 12 hours for up to 3 weeks vs. daily for 5 or 7 days.</p>
4	<p>Reluri (Guaifenesin, Phenylephrine) Tablet, 1200 mg/30 mg</p> <p><u>Usual Dose</u> Take 1 tablet orally every 12 hours</p>	<p><u>Orthographic</u> Both names consist of 6 letters, 2 upstrokes ('R', 't' in Rectiv and 'R', 'l' in Reluri) and start with the letter string 'Re-'. Additionally, the letter string '-iv-' in Rectiv may appear similar to the letter string '-er-' in Reluri when scripted.</p> <p><u>Strength</u> Single strength</p> <p><u>Numerical Overlap in the Usual Dose</u> 1 inch vs. 1 tablet</p> <p><u>Frequency of Administration</u> Every 12 hours</p>	<p><u>Orthographic</u> The name Reluri appears longer than the name Rectiv when scripted because of the presence of the letter string '-ur-' in Reluri.</p> <p><u>Dosage Form</u> Ointment vs. tablet</p> <p><u>Route of Administration</u> Topical vs. oral</p>

5	<p>Rebif (Interferon Beta-1a) Solution for injection 22 mcg/0.5 mL, 44 mcg/0.5 mL</p> <p><u>Usual Dose</u> Inject 22 or 44 mcg 3 times weekly subcutaneously.</p>	<p><u>Orthographic</u> Both names start with the letter string 'Re-'.</p> <p><u>Strength</u> Single strength</p> <p><u>Numerical Overlap in the Usual Dose</u> 1 inch vs. 1 tablet</p>	<p><u>Orthographic</u> 2 upstrokes ('R', 't') in Rectiv vs. 3 upstrokes ('R', 'b', 'f') in Rebif. Additionally, the letter suffix '-tiv' in Rectiv does not appear similar to the suffix '-bif' in Rebif when scripted.</p> <p><u>Strength</u> 0.4% vs. 22 mcg/0.5 mL and 44 mcg/0.5 mL</p> <p><u>Dosage Form</u> Ointment vs. solution for injection</p> <p><u>Route of Administration</u> Topical vs. subcutaneous</p> <p><u>Frequency of Administration</u> Every 12 hours vs. 3 times weekly</p> <p><u>Usual Dose</u> 1 inch vs. 22 to 44 mcg</p>
6	<p>Primlev (Oxycodone HCL and Acetaminophen) Tablet 5 mg/300 mg, 7.5 mg/300 mg, 10 mg/300 mg</p> <p><u>Usual Dose</u> Take 1 to 2 tablets (5 to 10 mg) orally every 6 hours as needed.</p>	<p><u>Orthographic</u> The letter strings 'Re-' and '- tiv' in Rectiv may appears similar to the letter strings 'Pr-' and '-lev' in Primleve when scripted.</p> <p><u>Partial Numerical overlap in the Usual Dose</u> 1 inch vs. 1 tablet</p>	<p><u>Orthographic</u> The name Primlev appears longer than the name Rectiv when scripted because of the presence of an additional letter, letter 'm' in Primlev.</p> <p><u>Strength</u> 0.4% vs. 5 mg/300 mg, 7.5 mg/300 mg, 10 mg/300 mg</p> <p><u>Dosage Form</u> Ointment vs. tablet</p> <p><u>Route of Administration</u> Topical vs. oral</p>
7	<p>Revatio (Sildenafil) Oral solution or tablet 10 mg/12.5 mL, or 20 mg</p> <p><u>Usual Dose</u> Take 20 mg orally three times daily.</p>	<p><u>Orthographic</u> Both names start with the letter string 'Re-' and contain the letter string '-ti-'.</p> <p><u>Strength</u> Single strength</p> <p><u>Numerical Overlap in the Usual Dose</u> 1 inch vs. 1 tablet</p>	<p><u>Orthographic</u> The name Revatio appears longer when scripted because of an extra letter and the rounded letter 'o' present in Revatio.</p> <p><u>Dosage Form</u> Ointment vs. tablet</p> <p><u>Route of Administration</u> Topical vs. oral</p> <p><u>Frequency of Administration</u> Every 12 hours vs. 3 times daily</p>

8	<p>Restasis (Cyclosporine) Emulsion, Drops 0.05%</p> <p><u>Usual Dose</u> Instill one drop into affected eye(s) twice daily approximately 12 hours apart.</p>	<p><u>Orthographic</u> The letter string 'Rect-' in Rectiv may appear similar to the letter string 'Rest-' in Restasis when scripted.</p> <p><u>Strength</u> Single strength</p> <p><u>Numerical Overlap in the Usual Dose</u> 1 inch vs. 1 drop</p> <p><u>Frequency of Administration</u> Every 12 hours</p>	<p><u>Orthographic</u> The name Restasis appears longer than the name Rectiv when scripted because of the presence of 2 additional letters in Restasis.</p> <p><u>Dosage Form</u> Ointment vs. drops</p> <p><u>Route of Administration</u> Topical vs. ocular</p>
9	<p>Videx (Didanosine) Capsule 125 mg, 200 mg, 250 mg, 400 mg,</p> <p><u>Usual dose</u> If greater than or equal to 60 kg: 400 mg orally once daily, if greater than 60 kg: 250 mg orally once daily, if 25 kg: 200 mg orally once daily.</p>	<p><u>Orthographic</u> The letter string '-ctiv' in Rectiv may appear similar to the letter string '-dex' in Videx when scripted.</p>	<p><u>Orthographic</u> The first letter 'R' does not appear similar to the first letter 'V' in Videx when scripted.</p> <p><u>Dosage Form</u> Ointment vs. capsule</p> <p><u>Route of Administration</u> Topical vs. oral</p> <p><u>Strength</u> 0.4% vs. 125 mg, 200 mg, 250 mg, 400 mg</p> <p><u>Frequency of Administration</u> Every 12 hours vs. once daily</p> <p><u>Usual Dose</u> 1 inch vs. varies with patients' weight</p>
10	<p>Rela (Carisoprodol) Tablet 250 mg, 350 mg (Discontinued, but generic equivalent is available)</p> <p><u>Usual Dose</u> Take 250 mg to 350 mg orally 3 to 4 times daily.</p>	<p><u>Orthographic</u> Both names start with the letter string 'Re-' and consist of 2 upstrokes ('R', 't' in Rectiv and 'R', 'l' in Rela).</p> <p><u>Partial Numerical Overlap in the Usual Dose</u> 1 inch vs. 1 tablet</p>	<p><u>Orthographic</u> The name Rectiv appears longer when scripted because of the presence of 2 extra letters in Rectiv. Additionally, the name Rela is discontinued.</p> <p><u>Dosage Form</u> Ointment vs. tablet</p> <p><u>Route of Administration</u> Topical vs. oral</p> <p><u>Strength</u> 0.4% vs. 250 mg, 350 mg</p> <p><u>Frequency of Administration</u> Every 12 hours vs. 3 to 4 times daily</p>

<p>11</p>	<p>Reclast (Zoledronic Acid) Solution for injection 5 mg/100 mg</p> <p><u>Usual Dose</u> Infuse 4 mg intravenously over a minimum of 15 minutes.</p>	<p><u>Orthographic</u> The letter string 'Rect-' in Rectiv may appear similar to the letter string 'Recl-' in Reclast when scripted</p> <p><u>Strength</u> Single strength</p>	<p><u>Orthographic</u> The suffix '-iv' in Rectiv does not appear similar to the letter string '-ast' in Reclast when scripted. Additionally, There are two upstrokes in Rectiv (‘R’, ‘t’) vs. 3 upstrokes (‘R’, ‘l’, ‘t’) in Reclast.</p> <p><u>Dosage Form</u> Ointment vs. solution for injection</p> <p><u>Route of Administration</u> Topical vs. intravenous</p> <p><u>Frequency of Administration</u> Every 12 hours vs. over minimum of 15 minutes</p> <p><u>Usual Dose</u> 1 inch vs. 4 mg</p>
<p>12</p>	<p>Replax (Eletriptan HBR) Tablet, 20 mg, 40 mg</p> <p><u>Usual Dose</u> Take 20 to 40 mg orally as a single dose as early as possible after the onset of symptoms.</p>	<p><u>Orthographic</u> Both names consist of 6 letters and start with the letter string ‘Re-’.</p> <p><u>Partial Numerical Overlap in the Usual Dose</u> 1 inch vs. 1 tablet</p>	<p><u>Orthographic</u> The presence of the down stroke ‘p’ in Replax may help differentiate the two names.</p> <p><u>Dosage Form</u> Ointment vs. tablet</p> <p><u>Route of Administration</u> Topical vs. oral</p> <p><u>Strength</u> 0.4% vs. 20 mg, 40 mg</p> <p><u>Frequency of Administration</u> Every 12 hours vs. once as a single dose at onset of symptoms</p>

<p>13</p>	<p>Relistor (Methylnaltrexone Bromide) Solution for injection 12 mg/0.6 mL</p> <p><u>Usual Dose</u> If greater than 38 kg: 0.15 mg/kg, if less than 62 kg: 8 mg, if between 62 to 114 kg: 12 mg, if greater than 114 kg: 0.15 mg subcutaneously every other day as needed.</p>	<p><u>Orthographic</u> Both names start with the letter string 'Re-'. Additionally, the letter string '-ti-' in Rectiv may appear similar to the letter string '-li-' in Relistor when scripted.</p> <p><u>Strength</u> Single strength</p>	<p><u>Orthographic</u> The name Relistor appears longer than the name Rectiv when scripted because of the extra two letters present in Relistor.</p> <p><u>Dosage Form</u> Ointment vs. solution for injection</p> <p><u>Route of Administration</u> Topical vs. subcutaneously</p> <p><u>Frequency of Administration</u> Every 12 hours vs. every other day as needed</p> <p><u>Usual Dose</u> 1 inch vs. varies based on patients weight</p>
<p>14</p>	<p>Relafen (Nabumetone).Tablet 500 mg, 750 mg (Discontinued, but generic equivalent is available)</p> <p><u>Usual Dose</u> Take 500 to 750 mg orally once or twice daily.</p>	<p><u>Orthographic</u> Both names start with the letter string 'Re-'. <u>Partial Numerical Overlap in the Usual Dose</u> 1 inch vs. 1 tablet <u>Partial Overlap in the Frequency of Administration</u> Twice daily</p>	<p><u>Orthographic</u> 2 upstrokes ('R', 't') in Rectiv vs. 3 upstrokes ('R', 'l', 'f') in Relafen. Additionally, the name Relafen appears longer than the name Rectiv because of an extra letter present in Relafen.</p> <p><u>Dosage Form</u> Ointment vs. tablet</p> <p><u>Route of Administration</u> Topical vs. oral</p> <p><u>Strength</u> 0.4% vs. 500 mg, 750 mg</p>

15	<p>Vectibix (Panitumumab) Solution for injection 20 mg/mL</p> <p>Usual Dose Infuse 6 mg/kg intravenously every 2 weeks.</p>	<p><u>Orthographic</u> Both names share the letter string '-ecti-'.</p> <p><u>Strength</u> Single strength</p>	<p><u>Orthographic</u> 2 upstrokes ('R', 't') in Rectiv vs. 3 upstrokes ('V', 't', 'b') in Vectibix. Additionally, the name Vectibix appears longer than the name Rectiv because of two extra letters present in Vectibix. Also, the first letter 'R' in Rectiv does not appear similar to the first letter 'V' in Vectibix when scripted.</p> <p><u>Dosage Form</u> Ointment vs. solution for injection</p> <p><u>Route of Administration</u> Topical vs. intravenous</p> <p><u>Frequency of Administration</u> Every 12 hours vs. every 2 weeks</p> <p><u>Usual Dose</u> 1 inch vs. 6 mg/kg</p>
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Appendix G: Potentially confusing names of topical products, but analysis indicates low potential for confusion

<p>PROPOSED NAME: Rectiv (Nitroglycerin) Ointment</p>	<p>STRENGTH: 0.4%</p>	<p>USUAL DOSE: Apply 1 inch ointment rectally every 12 hours up to 3 weeks.</p>
<p>FAILURE MODE: Name Confusion</p>	<p>CAUSES: (Potential reasons for name confusion that could lead to medication error)</p>	<p>PREVENTION OF FAILURE MODE (Reasons why the risk of medication error is minimized)</p>
<p>I Retin A (Tretinoin) Cream 0.25%, 0.05%, 0.1%</p> <p><u>Usual Dose</u> Apply topically once daily at bedtime</p>	<p><u>Orthographic</u> Both names share the letter string 'Re-'. Additionally, the letter string '-tiv' in Rectiv may appear similar to the letter string '-tin' in Retin A when scripted.</p> <p><u>Route of Administration</u> Topical</p>	<p><u>Orthographic</u> The modifier 'A' in Retin A, may help differentiate the two names.</p> <p><u>Strength</u> 0.4% vs. 0.25%, 0.05%, 0.1%</p>

2	<p>Rectorex (Hypericum Perforate, Ranunculus Ficaria, Symphytum Officinale, Matricaria, Chamomilla, Hamamelis Virginianum) Balm (Herbal Product)</p> <p><u>Usual Dose</u> Apply to the affected area rectally 2 to 3 times per day</p>	<p><u>Orthographic</u> Both names contain the letter string 'Rect-'. <u>Strength</u> Single strength <u>Route of Administration</u> Topical <u>Overlap in the Frequency of Administration</u> 2 times</p>	<p><u>Orthographic</u> 6 letters in Rectiv vs. 8 letters in Rectorex, therefore the name Rectorex appears longer than Rectiv when scripted. Additionally, the cross letter 'x' in Rectorex may help differentiate the two names.</p>
3	<p>Proactiv (Acne treatment in multiple formulations)</p> <p><u>Usual Dose</u> Apply once or twice daily topically.</p>	<p><u>Orthographic</u> Both names contain the letter string '-ctiv'. <u>Route of Administration</u> Topical <u>Strength</u> Single strength <u>Overlap in the Frequency of Administration</u> 2 times</p>	<p><u>Orthographic</u> 6 letters in Rectiv vs. 8 letters in Proactiv, therefore Proactiv appears longer than Rectiv when scripted. Additionally, the placement of the upstroke 't' may help differentiate the two names (4th position in Rectiv vs. 6th position in Proactiv)</p>
4	<p>Veltin (Clindamycin Phosphage, Tretinoin) Topical gel 1.2%-0.025%</p> <p><u>Usual Dosage</u> Apply to affected areas topically once daily at bedtime.</p>	<p><u>Orthographic</u> Both names consist of 6 letters. Additionally, the letter string '-tiv' in Rectiv may appear similar to the letter string '-tin' in Veltin when scripted <u>Strength</u> Single strength <u>Route of Administration</u> Topical</p>	<p><u>Orthographic</u> 2 upstrokes ('R', 't') in Rectiv vs. 3 upstrokes ('V', 'l', 't') in Veltin. <u>Frequency of Administration</u> Every 12 hours vs. once at bedtime</p>

5	<p>Rectasol HC (Hydrocortisone) Suppository, 25 mg</p> <p><u>Usual Dose</u> Insert 1 suppository rectally twice daily in the morning and in the evening for 2 weeks</p>	<p><u>Orthographic</u> Both names start with the letter string 'Rect-'.</p> <p><u>Strength</u> Single strength</p> <p><u>Route of Administration</u> Rectal</p> <p><u>Numerical Overlap in the Usual Dose</u> 1 inch vs. 1 suppository</p> <p><u>Frequency of Administration</u> Twice daily</p>	<p><u>Orthographic</u> 6 letters in Rectiv vs. 8 letters in Rectasol (without the modifier HC), therefore the name Rectasol appears longer than Rectiv when scripted. Additionally, if included, the modifier 'HC' may help differentiate the two names.</p> <p><u>Dosage Form</u> Ointment vs suppository</p>
6	<p>Recort (Hydrocortisone) Ointment, 1%</p> <p><u>Usual Dose</u> Apply to the affected area topically 2 to 4 times per day.</p>	<p><u>Orthographic</u> Both names consist of 6 letters and start with the letter string 'Rec-'. Additionally they both contain the upstrokes 'R' and 't'.</p> <p><u>Strength</u> Single strength</p> <p><u>Route of Administration</u> Topical</p> <p><u>Overlap in the Frequency of Administration</u> 2 times daily</p>	<p><u>Orthographic</u> The placement of the upstroke 't' may help differentiate the two names (4th position in Rectiv vs. 6th position in Recort)</p>
7	<p>Rectagel HC (Lidocain and Hydrocortisone) gel 2.8%, 0.55%</p> <p><u>Usual Dose</u> Apply to the affected area rectally 2 to 3 times per day.</p>	<p><u>Orthographic</u> Both names start with the letter string 'Rect-'.</p> <p><u>Strength</u> Single strength</p> <p><u>Route of Administration</u> Topical</p> <p><u>Overlap in the Frequency of Administration</u> 2 times daily</p>	<p><u>Orthographic</u> 6 letters in Rectiv vs. 8 letters in Rectagel. 2 upstrokes ('R', 't') and no down strokes in Rectiv vs. 3 upstrokes ('R', 't', 'l') and one downstroke ('g') in Rectagel. Additionally, if included, the modifier 'HC' may help differentiate the two names.</p>

8	<p>Rectacaine (Phenylephrine) Ointment, 0.25%</p> <p><u>Usual Dose</u> Apply to the affected area rectally up to 4 times daily.</p>	<p><u>Orthographic</u> Both names start with the letter string 'Rect-'. <u>Strength</u> Single strength <u>Route of Administration</u> Topical <u>Overlap in the Frequency of Administration</u> 2 times daily (Rectacaine may be applied only 2 times daily)</p>	<p><u>Orthographic</u> 6 letters in Rectiv vs. 10 letters in Rectacaine.</p>
9	<p>Vectical (Calcitriol) Ointment 3mcg/gram</p> <p><u>Usual Dose</u> Apply topically to the affected area twice daily.</p>	<p><u>Orthographic</u> Both names share the letter string '-ecti-'. <u>Strength</u> Single strength <u>Route of Administration</u> Topical <u>Frequency of Administration</u> Twice daily</p>	<p><u>Orthographic</u> 2 upstrokes ('R', 't') in Rectiv and 3 upstrokes ('V', 't', 'l') in Vectical. Additionally the first letter 'R' in Rectiv does not appear similar to the first letter 'V' in Vectical when scripted. Also, the name Vectical has 8 letters vs. 6 letters in Rectiv and therefore Vectical appears longer when scripted.</p>

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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

Date: December 28, 2009

To: Bob Rappaport, MD, Director
Division of Anesthesia, Analgesia and Rheumatology Products

Through: Kristina C. Arnwine, PharmD, Team Leader
Denise Toyer, Pharm.D., Deputy Director
Division of Medication Error Prevention and Analysis (DMEPA)

From: Tselaine Jones Smith, PharmD, Safety Evaluator
Division of Medication Error Prevention and Analysis (DMEPA)

Subject: Proprietary Name Review

Drug Name(s): Cellegesic (Nitroglycerin Ointment, USP) 0.4%

Application Type/Number: NDA 021359

Applicant/Applicant: ProStrakan Inc.

OSE RCM #: 2009-1999

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

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EXECUTIVE SUMMARY

Cellegesic is the proposed proprietary name for Nitroglycerin Ointment, USP. This proposed name was evaluated from a safety and promotional perspective based on the product characteristics provided by the Applicant. We sought input from pertinent disciplines involved with the review of this application and considered it accordingly.

Our evaluation finds the proposed name, Cellegesic, is vulnerable to name confusion with the currently marketed products Calagesic and Alagesic, because of the phonetic and orthographic similarities and overlapping product characteristics shared by these name pairs. Thus, we do not recommend the use of the proposed proprietary name, Cellegesic, for this product and have provided comments in Section 4 explaining our analysis.

1 BACKGROUND

1.1 INTRODUCTION

This review is in response to the September 30, 2009 submission from ProStrakan, Inc. for an assessment of the proposed proprietary name, Cellegesic, for its promotional nature and the potential to contribute to medication errors. ProStrakan submitted container labels, carton and insert labeling which will be reviewed under separate cover.

1.2 REGULATORY HISTORY

Cellgey Pharmaceuticals, Inc. initially submitted the proposed proprietary name, Cellegesic (Nitroglycerin Ointment, USP), 0.4% for NDA 021359 on June 30, 2004. DMEPA reviewed and had no objection to the proposed proprietary name, Cellegesic, for this product in OSE Review # 01-0092-2. The NDA received a non-approvable letter on December 23, 2004. The non-approvable letter did not contain references to the acceptability of the proprietary name. In the fourth quarter of 2006, Cellgey sold the NDA, including the US rights, for Cellegesic to ProStrakan Incorporated. ProStrakan resubmitted the NDA on September 30, 2009.

1.3 PRODUCT INFORMATION

Cellegesic (Nitroglycerin Ointment, USP) 0.4% is indicated for the treatment of moderate to severe pain associated with chronic anal fissures. The recommended dose is 375 mg (equivalent to 1.5 mg of nitroglycerin) intra-anally approximately every 12 hours. Treatment should be continued for up to three weeks. Cellegesic will be supplied in 30 gram tubes.

The following steps should be taken to administer the correct dose of Cellegesic:

1. Place a finger covering, such as plastic wrap, disposable glove or finger cot on the finger to apply ointment.
2. To obtain a 375 mg dose, the covered finger is laid along side a 1 inch dosing line on the carton.
3. Express a line of ointment onto until the covered finger that is the length of the measuring line.
4. The ointment is gently inserted into the anal canal using the covered finger no further than to the first finger joint and the ointment is applied around the side of the anal canal.
5. Hand should be washed after administration.

The proposed route of administration for this product is 'intra-anal'; however, this has not been finalized.

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 and 2.2 identify specific information associated with the methodology for the proposed proprietary name, Cellegesic.

2.1 SEARCH CRITERIA

For this review, particular consideration was given to drug names beginning with the letter 'C' 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.^{3,4}

To identify drug names that may look similar to Cellegesic, the DMEPA staff also considers the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (ten letters), upstrokes (three, capital letter 'C', and lower case 'l'), down strokes (one, lower case 'g'), cross strokes (none), and dotted letters (one, lower case 'i'). Additionally, some letters in Cellegesic may be vulnerable to ambiguity when scripted (See Appendix B). As a result, the DMEPA staff also considers these alternate appearances when identifying drug names that may look similar to Cellegesic.

When searching to identify potential names that may sound similar to Cellegesic, the DMEPA staff searches for names with similar number of syllables (four), stresses (CELL-e-ge-sic), cell-E-ge-sic, cell-e-GE-sic or cell-e-ge-SIC) and placement of vowel and consonant sounds. Additionally, the DMEPA staff considers that pronunciation of parts of the name can vary. For example, 'C' may sound like 'S' or 'Z'. Likewise, 'e' may sound like 'ä'; 'ge' may sound like 'gee'; 's' may sound like 'z' and 'c' may sound like 'ck' and '-sic' may sound like '-zic'. (See Appendix B).

The Applicant's intended pronunciation of the proprietary name is presented as sell-eh-GEE-sic. However, names are often mispronounced and/or spoken with regional accents and dialects, so other potential pronunciations of the name 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 medication order, outpatient and verbal prescription was communicated during the FDA prescription studies.

³ Institute for Safe Medication Practices. Confused Drug name List (1996-2006). Available at <http://www.ismp.org/Tools/confuseddrugnames.pdf>

⁴ Kondrack, G and Dorr, B. Automatic Identification of Confusable Drug Names. Artificial Intelligence in Medicine (2005)

Figure 1. Cellegesic Study (conducted on October 29, 2009)

HANDWRITTEN PRESCRIPTION ORDERS	VERBAL PRESCRIPTION ORDER
<p><u>Inpatient Prescription Order:</u> <i>Cellegesic apply inside the anus BID</i></p>	<p>Cellegesic #1 Apply to the inside of the anus twice a day</p>
<p><u>Outpatient Prescription Order:</u> <i>Cellegesic #1 use as directed</i></p>	

3 RESULTS

3.1 DATABASE AND INFORMATION SOURCES

The searches yielded a total of sixteen names as having some similarity to the name Cellegesic.

Fourteen of the names were thought to look like Cellegesic. These include Duragesic, Paregoric, Cellcept, Norgesic, Celebrex, Percogesic, Collengenase, Allegra, Allergen, Alagesic, Ceterizine, Cellsure, Cellugel and Valergen. The remaining 2 names, Calagesic and Caligesic, were thought to look and sound like Cellegesic.

Additionally, DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of December 3, 2009.

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 Cellegesic.

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 ANALYSIS STUDIES

A total of 22 practitioners responded. Seven (n=7) of the responses overlapped with the existing drug name Alagesic. Five (n=5) of the participants interpreted the name correctly as 'Cellegesic'. The remainder of the respondents misinterpreted (n=17) the drug name. In the inpatient written study, respondents misinterpreted name 'Cellegesic' as 'Allegesic' which is similar to the existing drug name Alagesic. In the verbal prescription studies, the letter 'C' was misinterpreted as the letter 'S', there was omission of a 'l' and '-sic' was misinterpreted as the letters '-zic'. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

3.4 COMMENTS FROM THE DIVISION OF ANESTHESIA, ANALGESIA AND RHEUMATOLOGY PRODUCTS (DAARP)

3.4.1 Initial Phase of Review

In response to the OSE email on October 29, 2009, DAARP did not forward any comments and/or concerns on the proposed name at the initial phase of the name review. However, they did note concerns with the efficacy of the product.

3.4.2 Midpoint of Review

DMEPA notified the Division via e-mail that we had objections to the proposed proprietary name, Cellegesic, on December 24, 2009. Per e-mail correspondence from the Division on December 24, 2009, they indicated they concur with our assessment of the proposed proprietary name, Cellegesic.

3.5 SAFETY EVALUATOR RISK ASSESSMENT

Independent searches by the primary Safety Evaluator identified one name, Alfusozin, which was thought to look similar to Cellegesic and represent a potential source of drug name confusion.

4 DISCUSSION

Neither DDMAC nor the review Division had concerns with the proposed name.

A total of 17 names were identified as potential sources of drug name confusion with Cellegesic.

Of the 17 names, three names were eliminated from further analysis for the following reasons. One name lacked orthographic and/or phonetic similarity, one name was a drug product that is no longer marketed and has no generic equivalents available and one name is a product that is not a drug and is used for research purpose (see Appendices D through F).

Failure mode and effect analysis (FMEA) was then applied to determine if the proposed proprietary name could potentially be confused with the remaining 14 names and lead to medication errors. This analysis determined that the name similarity between Cellegesic and 12 of the 14 products was unlikely to result in medication errors for the reasons presented in Appendix G. However, the similarity between the proposed name Cellegesic and the currently marketed products Calagesic and Alagesic makes Cellegesic vulnerable to name confusion that could lead to medication errors for the following reasons.

4.1 CALAGESIC NAME CONFUSION

The proposed proprietary name Cellegesic is orthographically and phonetically similar to the name Calagesic. Calagesic is the proprietary name for calamine and pramoxine lotion, 8%/1%. It is indicated for the relief of itching associated with insect bites, sunburn or poison ivy. The product is applied to the affected areas three to four times a day.

Although Cellegesic has the double letter 'll' in the middle of the name and Calagesic has a single letter 'l', they are presented in the same position in each name. Furthermore, the names have identical beginnings ('C-') and endings ('-gesic') and the remaining letters ('-elle' vs. '-ala') are orthographically similar when scripted. Phonetically, both names have four syllables and the sound of the hard 'C' name Calagesic can be mispronounced with a soft 'C' (i.e., Salagesic) which makes it difficult to discern the name from Cellegesic when spoken.

*Cellegesic
Calagesic*

In addition to the orthographic and phonetic similarities of this name pair, Cellegesic and Calagesic are single strength products and share similar dosage forms (ointment/lotion) and routes of administration (topical), which makes it possible for prescribers to omit the strength and dosage form when writing orders for these products. Furthermore, despite the different dosing (1 inch vs. sufficient amount) and frequencies of administration (every 12 hours vs. three to four times daily), prescribers may write 'use as directed' on written orders for either product which also increases the potential for confusion between this name pair. Although Calagesic is available as an 'over-the-counter' (OTC) product, it is not uncommon for practitioners to write prescriptions for 'OTC' products in a hospital-based practice or to reinforce verbal recommendations to a patient.

4.2 ALAGESIC NAME CONFUSION

The proposed name Cellegesic is orthographically similar to the name Alagesic. Alagesic is the proprietary name for acetaminophen, butabital and caffeine, 325 mg/50 mg/40 mg. It is indicated for the relief of the symptomatic complex of tension or muscle contraction headache. The recommended dose is one to two tablets orally every four hours as needed.

When scripted, the letters 'Ce' of Cellegesic can look like the capital letter 'A' of Alagesic. Although Cellegesic has the double letter 'll' in the middle of the name and Alagesic has a single letter 'l', they are presented in the same position in each name. In addition, the names have identical endings ("-gesic") which can lead to further confusion when the names are scripted. Moreover, in the FDA Prescription Analysis, respondents in the written studies misinterpreted the name 'Cellegesic' as 'Allegesic', which is similar to the name Alagesic. Alagesic can be inadvertently dispensed if Cellegesic is ordered and misinterpreted as Allegesic and considered a misspelling of Alagesic or vice-a-versa.

*Cellegesic
Alagesic*

*Cellegesic 1" q0h
Alagesic 1 q0h*

In addition to the orthographic similarity of this name pair, Cellegesic and Alagesic are single strength products, which makes it possible for prescribers to omit the strength when writing orders for these products. Furthermore, both products overlap with regards to dose (one inch vs. one tablet). However, if the dose for Cellegesic is written as "1", the abbreviation used to represent inch may be overlooked and the dose misinterpreted as 1 (representing one tablet). Despite the different frequency of administration an order for "Cellegesic 1" every 12 hours" could be misinterpreted as "Alagesic 1 (tablet) every 12 hours."

5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment found the proposed name Cellegesic unacceptable from a safety perspective due to its similarity to the currently marketed products Calagesic and Alagesic.

If you have further questions or need clarifications, please contact Bola Adeolu or Cherye Milburn, Regulatory Project Managers, at 301-796-4264 or 301-796-2084, respectively.

5.1 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, Cellegesic, and have concluded that it is unacceptable for the following reasons.

1. Cellegesic is orthographically and phonetically similar to and shares overlapping characteristics with the proprietary name Calagesic. The orthographic similarity of this name pair is attributed to the shared beginning and ending letters ("C and gesic") and the similar appearance of the remaining letters when scripted. These similarities are demonstrated in the scripted samples provided below.



The image shows two lines of handwritten text. The top line reads "Cellegesic" and the bottom line reads "Calagesic". The letters are written in a cursive, slanted style, highlighting the orthographic similarities between the two names.

This name pair may sound similar because the beginning letter in Calagesic may be mispronounced with an 'S' sound and both names have four syllables with multiple overlapping letters in a similar sequence. Both products may be prescribed with a signatura of 'use as directed' on a medication order or prescribed in terms of the number of tubes or bottles (i.e., one). Consequently, we believe a prescription for "Cellegesic use as directed #1" could be misinterpreted as "Calagesic use as directed #1" or vice versa. Thus, the quantity indicated on a prescription may provide further confirmation for misinterpretation of the prescription. Additionally, both products are available in a single strength thus the strength may not be a distinguishing characteristic since the product strength is not required for dispensing either product. Although Calagesic is available as an 'over-the-counter' (OTC) product, it is not uncommon for practitioners to write prescriptions for 'OTC' products in a hospital-based practice or to reinforce verbal recommendations to a patient. The orthographic and phonetic similarities of this name pair coupled with product characteristic similarities create the potential for wrong drug medication errors that may occur during transcribing, order entry and dispensing of the drug product.

2. The proposed name Cellegesic is orthographically similar to the name Alagesic. The orthographic similarity of this name pair is attributed to the similar appearance of the beginning letters and the shared ending 'gesic.' These similarities are demonstrated in the scripted samples provided below.



The image shows two columns of handwritten text. The left column has "Cellegesic" on top and "Alagesic" on the bottom. The right column has "Cellegesic 1 inch" on top and "Alagesic 1" on the bottom. The handwriting is cursive and slanted, illustrating the orthographic similarities between the two name pairs.

Both are single strength products, indicated for pain relief and overlap with regards to the dose (one inch vs. one tablet). However, if the dose for Cellegesic is written as 1", the abbreviation used for inch may be overlooked and the dose misinterpreted as 1 (representing one tablet). Despite the different frequency of administration an order for "Cellegesic 1" every 12 hours" could be misinterpreted as "Alagesic 1 (tablet) every 12 hours." The orthographic similarities of this name pair

coupled with product characteristic similarities create the potential for wrong drug medication errors that may occur during transcribing, order entry and dispensing of the drug 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. *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)*

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)*

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)*

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)*

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)*

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.⁵

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

⁵ National Coordinating Council for Medication Error Reporting and Prevention.
<http://www.nccmerp.org/aboutMedErrors.html>. Last accessed 10/11/2007.

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.⁶ 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.⁷ DMEPA provides the product characteristics considered for this review in section one.

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 Applicant’s intended pronunciation of the proprietary name. However, DMEPA also considers a variety of pronunciations that could occur in the English language because the Applicant has little control over how the name will be spoken in clinical practice.

⁶ Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

⁷ 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	<ul style="list-style-type: none"> Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication Names may look similar when scripted and lead to drug name confusion in written communication
	Orthographic similarity	Similar spelling Length of the name Upstrokes Down strokes Cross-strokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	<ul style="list-style-type: none"> Names may look similar when scripted, and lead to drug name confusion in written communication
Sound-alike	Phonetic similarity	Identical prefix Identical infix Identical suffix Number of syllables Stresses Placement of vowel sounds Placement of consonant sounds Overlapping product characteristics	<ul style="list-style-type: none"> Names may sound similar when pronounced and lead to drug name confusion in verbal communication

Lastly, 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.

5. 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.

5. 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 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.

5. 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.⁸ 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?”

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)].

⁸ Institute for Healthcare Improvement (IHI). Failure Mode and Effects Analysis. Boston. IHI:2004.

- 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 Applicant 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 Applicant 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. 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), Joint Commission on Accreditation of Hospitals (JCOAH), 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 Applicant 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. Applicants have undertaken higher-leverage strategies, such as drug name changes, in the past but at great financial cost to the Applicant 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 Applicants' 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).

Appendix B: Letters with possible orthographic or phonetic misinterpretation

Letters in Name, Cellegesic	Scripted may appear as	Spoken may be interpreted as
Capital 'C'	'A', 'G', 'L', or 'E'	'S', 'Z'
lower case 'e'	'i', 'o', 'a'	
lower case 'l'	'j'	
lower case 'l'	'i'	
lower case 'e'	'i', 'o', 'a'	ă
lower case 'g'	'p', 'y', 'j', 'z'	
lower case 'e'	'i', 'o', 'a'	
lower case 's'	'n', 'r'	'z'
lower case 'i'	'e'	
lower case 'c'	'r', 's'	'ck', 'c'
lower case 'le'	'b'	
lower case 'sic'	'-zic'	'sick', 'zick'
lower case 'ic'	'u'	

Appendix C: FDA Prescription Study Responses

Inpatient Prescription	Outpatient Prescription	Voice Prescription
Allegesic	Cellegesic	Selogesic
Allegesic	Collegesic	Celagesic
Allegesic	Cellegesic	Celegesic
Allegesic	Cellegesic	Seligesic
Allegesic	Cellegesic	Selegesic
Allegesic	Cellegesic	Celegesic
Allegesic		Selagezic
Allegesic		
Allegesic		

Appendix D: Names Lacking Orthographic and/or Phonetic Similarity.

Name	Similarity to Cellegesic
Norgesic	Look

Appendix E: Drug products that are discontinued and no generic equivalent is available

Proprietary Name	Similarity to Cellegesic	Status and Date
(b) (4)		

Appendix F: Product that is a used in a laboratory by researchers

Proprietary Name	Similarity to Cellegesic	Strength	Signa
Cellegesic (nitroglycerin ointment, USP)		0.4%	375 mg (1 inch) intra-anally approximately every 12 hours
Cellsure cDNA kit*	Look	N/A	Cellsure is normally used for research purposes by microbiologist in laboratory settings who perform reverse transcription reactions on a small population of cells Orders for Cellsure would not be seen in inpatient or outpatient settings

(b) (4)

Appendix G: Products with orthographic, phonetic and/or multiple differentiating product characteristics minimize the potential for medication errors in the usual practice settings

Product name with potential for confusion	Similarity to Cellegesic	Strength	Usual Signa (if applicable)	Differentiating Product Characteristics
Cellegesic (nitroglycerin ointment, USP)		0.4%	375 mg (1 inch) intranasally approximately every 12 hours	
Duragesic (fentanyl hydrochloride) transdermal system	Look	12 mcg/hour 25 mcg/hour 50 mcg/hour 75 mcg/hour 100 mcg/hour	Apply 25 mcg/hour to 300 mcg/hour every 72 hours	The beginning letters 'Celle-' and the two upstrokes of the letter 'l' in Cellegesic differentiate it the beginning letters 'Dura-' of Duragesic when scripted Strength (0.4% vs. 12.5 mcg/hour, 25 mcg/hour, 50 mcg/hour, 75 mcg/hour, 100 mcg/hour) Frequency of administration (every 12 hours vs. every 72 hours)
Paregoric (Opium) liquid	Look	2 mg/5 mL (0.4 mg/mL)	5 mL to 10 mL orally once daily to four times per day	The beginning letters 'Celle-' and the two upstrokes of the letter 'l' in Cellegesic differentiate it the beginning letters 'Pare-' of Paregoric when scripted Route of administration (topical vs. oral) Frequency of administration (every 12 hours vs. four times a day) Dosage form (ointment vs. liquid)

Product name with potential for confusion	Similarity to Cellegesic	Strength	Usual Signa (if applicable)	Differentiating Product Characteristics
Cellegesic (nitroglycerin ointment, USP)		0.4%	375 mg (1 inch) intranally approximately every 12 hours	
Percogesic (acetaminophen and phenyltoloxamine) tablets	Look	Tablets: 325 mg/30 mg	One to two tablets every two to six hours as needed for pain	The beginning letters 'Celle-' and the two upstrokes of the letter 'l' in Cellegesic differentiate it from the letters 'Perco-' of Percogesic when scripted Route of administration (topical vs. oral) Frequency of administration (twice daily vs. every six hours or every four hours) Dosage form (ointment vs. caplet or tablet)
Cetirizine (Brand: Zyrtec)	Look	Syrup: 5 mg/5 mL Tablets: 5 mg, 10 mg Chewable tablets: 5 mg, 10 mg	5 mg to 10 mg orally once daily	Strength (0.4% vs. 5 mg/mL, 5 mg or 10 mg) Route of administration (topical vs. oral) Dosage form (ointment vs. tablets or syrup)

Product name with potential for confusion	Similarity to Cellegesic	Strength	Usual Signa (if applicable)	Differentiating Product Characteristics
Cellegesic (nitroglycerin ointment, USP)		0.4%	375 mg (1 inch) intranally approximately every 12 hours	
Valergen* (estradiol valerate) injection *Valergen is no longer available in the marketplace. However, there are generic versions of estradiol valerate injection	Look	10 mg/mL 20 mg/mL 40 mg/mL	10 mg to 20 mg intramuscularly every four weeks as necessary	Cellegesic looks longer than Valergen when scripted. Additionally, there are four letters after the downstroke of the letter 'g' in Cellegesic vs. 2 letters after the letter 'g' in Valergen. Strength (0.4% vs. 10 mg/mL, 20 mg/mL or 40 mg/mL) Dose (375 mg or 1 inch vs. 10 mg to 20 mg) Route of administration (intra-anal vs. intramuscular) Frequency of administration (twice daily vs. every four weeks) Dosage form (ointment vs. injection)
Collagenase ointment (established name for Santyl)	Look	250 units/gram	Apply a thin layer to the site once daily (or more) frequently if the dressing becomes soiled	The ending letters ('-ase') of Collagenase allows the name to look longer than Cellegesic when scripted

Product name with potential for confusion	Similarity to Cellegesic	Strength	Usual Signa (if applicable)	Differentiating Product Characteristics
Cellegesic (nitroglycerin ointment, USP)		0.4%	375 mg (1 inch) intranally approximately every 12 hours	
Cellcept (mycophenolate mofetil)	Look	Capsule: 250 mg Tablet: 500 mg Injection: 500 mg Oral suspension: 200 mg/mL	One (1) gram orally or intravenously twice daily	The ending letters ('-gesic') make the name Cellegesic appear longer than Cellcept when scripted. In addition, the cross stroke of the letter 't' at the end of Cellcept also helps to differentiate the names when scripted. Route of administration (topical vs. oral or intravenous) Dosage forms (ointment vs. capsule, tablet, injection or oral suspension)
Cellugel Ophthalmic viscosurgical device supplied in a disposable syringe delivering 2% hydroxypropyl methylcellulose (1 mL)	Look	2%	Inject device into the anterior chamber of the eye prior designed to create and maintain space to protect the corneal endothelium and other intraocular tissues during surgery	The ending letters ('-esic') allow the name Cellegesic to appear longer than Cellugel when scripted. Route of administration (topical vs. intraocular) Dosage form (ointment vs. solution for injection) Context of use (outpatient use vs. maintenance of intraocular space during eye surgery)

Product name with potential for confusion	Similarity to Cellegesic	Strength	Usual Signa (if applicable)	Differentiating Product Characteristics
Cellegesic (nitroglycerin ointment, USP)		0.4%	375 mg (1 inch) intranally approximately every 12 hours	
Allegra (fexofenadine hydrochloride)	Look	Tablets: 30 mg, 60 mg, 180 mg Oral suspension: 30 mg/5 mL (6 mg/mL) Orally disintegrating tablet: 30 mg	15 mg to 60 mg orally twice daily 180 mg orally once daily	The endings of the two names ('-sic' vs. '-a') differentiate the two names when scripted. In addition, the ten letters in Cellegesic allows it to look longer than the seven letters of Allegra when scripted Route of administration (intra-anal vs. oral) Strength (0.4% vs. 30 mg, 60 mg, 180 mg, 30 mg/5 mL) Dosage form (ointment vs. tablets, oral suspension)
Allergen Otic (antipyrine and benzocaine) solution	Look	54 mg/14 mg per mL	Otitis media pain: Instill 2 to 4 drops into ear canal(s), insert a saturated cotton plug, repeat 3 to 4 times per day or once every 1 to 2 hours Cerumen removal: Instill 3 to 4 drops per day for 2 to 3 days, after 2 to 3 days irrigate the ear canal with warm water	The addition of the modifier 'Otic' helps differentiate the two names when scripted The endings of the two names ('-sic' vs. '-n') differentiate the two names when scripted Dosage form (ointment vs. solution) Route of administration (topical vs. intraocular) Frequency of administration (twice daily vs. three to four times a day or once a day)

Product name with potential for confusion	Similarity to Cellegesic	Strength	Usual Signa (if applicable)	Differentiating Product Characteristics
Cellegesic (nitroglycerin ointment, USP)		0.4%	375 mg (1 inch) intranally approximately every 12 hours	
Celebrex (Celecoxib) capsules	Look	50 mg, 100 mg, 200 mg, and 400 mg	100 to 200 mg orally once daily	The ending letters ('-gesic') make the name Cellegesic appear longer than Celebrex when scripted. Strength (0.4% vs. 50 mg, 100 mg, 200 mg, and 400 mg) Route of administration (topical vs. oral) Dosage form (ointment vs. capsule)
Alfuzosin (established name for Uroxatral) extended release tablet Generic products have tentative approval* dates (drugs at FDA) (ANDA 79013, 79014, 79056, 79060, 90221, 90284)	Look	10 mg	10 mg orally immediately after the same meal each day	Alfuzosin looks longer than Cellegesic when scripted. The name Alfuzosin contains two downstrokes (the letters 'f' and 'z') which helps to differentiate it from Cellegesic which has only one downstroke when scripted Route of administration (topical vs. oral) Dosage form (ointment vs. tablet)

*Tentative approval: For those drugs that cannot be marketed in the United States due to existing patent protection, a so-called "tentative" approval is granted. Tentative approval means that existing patents or exclusivity prevent the product from being sold in the United States, but that the product meets all of the scientific and quality standards for marketing in the U.S
(<http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm>)

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-21359

ORIG-1

PROSTRAKAN INC

CELLEGESIC NITROGLYCERIN
OINTMENT 0.4%

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/s/

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