CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

204803Orig1s000

PROPRIETARY NAME REVIEW(S)

PROPRIETARY NAME REVIEW

Division of Medication Error Prevention and Analysis (DMEPA)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

***** This document contains proprietary information that cannot be released to the public*****

Date of This Review:	October 4, 2019
Application Type and Number:	NDA 204803
Product Name and Strength:	Posimir (bupivacaine) Extended-Release Solution, 132 mg/mL
Total Product Strength:	660 mg/5 mL
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Durect Corporation (Durect)
Panorama #:	2019-33088670
DMEPA Safety Evaluator:	Deborah Myers, RPh, MBA
DMEPA Team Leader:	Otto L. Townsend, PharmD

Contents

1 INTRODUCTION

This review evaluates the proposed proprietary name, Posimir, from a safety and misbranding perspective. The sources and methods used to evaluate the proposed proprietary name are outlined in the reference section and Appendix A respectively. Durect did not submit an external name study for this proposed proprietary name.

1.1 REGULATORY HISTORY

Durect previously submitted the proposed proprietary name, Posimir on September 24, 2012. We found the name, Posimir conditionally acceptable under IND 066086 on March 21, 2013.[a]

Subsequently, Durect submitted the proposed proprietary name, Posimir on April 25, 2013. We found the name, Posimir conditionally acceptable under NDA 204803 on July 22, 2013.[b]

The Agency issued a Discipline Response Letter (DRL) on January 14, 2014, followed by a Complete Response Letter (CRL) on February 12, 2014, to New Drug Application (NDA) 204803.

On June 26, 2019, Durect submitted their Complete Response to the Agency's February 12, 2014, CRL.

On July 2, 2019, the Agency sent an IR to Durect noting that their Class 2 Resubmission of NDA 204803 (received June 27, 2019) did not include a request for Proprietary Name Review. Subsequently, on July 12, 2019, Durect submitted their proposed proprietary name, Posimir, for review.

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on July 12, 2019.

- Intended Pronunciation: pah' si mir
- Active Ingredient: bupivacaine
- Indication of Use: Indicated for single-dose instillation into the surgical site to produce post-surgical analgesia.
- Route of Administration: instilled into the surgical site
- Dosage Form: Extended-Release Solution
- Strength: 132 mg/mL (660 mg/5 mL)
- Dose and Frequency: 5 mL (660 mg) once per surgical procedure

[a] Borders-Hemphill, V. Proprietary Name Review for Posimir (IND 066086). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2013 MAR 21. Panorama No. 2012-2280.

[b] Borders-Hemphill, V. Proprietary Name Review for Posimir (NDA 204803). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2013 JUL 22. Panorama No. 2013-1001.

- How Supplied: 5 mL single-dose vial, 660 mg/5 mL (13.2%, 132 mg/mL) packaged in a 10-unit carton
- Storage: Store at a controlled room temperature of 20°C to 25°C (68°F to 77°F) [See USP Controlled Room Temperature]. Vial should be protected from light and retained in carton until time of use.

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Posimir would not misbrand the proposed product. The Division of Medication Error Prevention and Analysis (DMEPA) and the Division of Anesthesia, Analgesia, and Addiction Products (DAAAP) concurred with the findings of OPDP's assessment for Posimir.

2.2 SAFETY ASSESSMENT

The following aspects were considered in the safety evaluation of the proposed proprietary name, Posimir.

2.2.1 United States Adopted Names (USAN) Search

There is no USAN stem present in the proposed proprietary name[c].

2.2.2 Components of the Proposed Proprietary Name

Durect did not provide a derivation or intended meaning for the proposed proprietary name, Posimir, in their submission. This proprietary name is comprised of a single word that does not contain any components (i.e. a modifier, route of administration, dosage form, etc.) that are misleading or can contribute to medication error.

2.2.3 Comments from Other Review Disciplines at Initial Review

In response to the OSE, July 24, 2019 e-mail, the Division of Anesthesia, Analgesia, and Addiction Products (DAAAP) did not forward any comments or concerns relating to Posimir at the initial phase of the review.

2.2.4 FDA Name Simulation Studies

Eighty-six practitioners participated in DMEPA's prescription studies for Posimir. The responses did not overlap with any currently marketed products nor did the responses sound or look similar to any currently marketed products or any products in the pipeline. Appendix B contains the results from the verbal and written prescription studies.

[c] USAN stem search conducted on July 16, 2019.

2.2.5 Phonetic and Orthographic Computer Analysis (POCA) Search Results

Our POCA search[d] identified 111 names with a combined phonetic and orthographic score of ≥55% or an individual phonetic or orthographic score ≥70%. These names are included in Table 1 below.

2.2.6 Names Retrieved for Review Organized by Name Pair Similarity

Table 1 lists the number of names retrieved from our POCA search. These name pairs are organized as highly similar, moderately similar or low similarity for further evaluation.

Table 1. Names Retrieved for Review Organized by Name Pair Similarity

Similarity Category	Number of Names
Highly similar name pair: combined match percentage score ≥70%	6
Moderately similar name pair: combined match percentage score ≥55% to ≤ 69%	97
Low similarity name pair: combined match percentage score ≤54%	8

2.2.7 Safety Analysis of Names with Potential Orthographic, Spelling, and Phonetic Similarities

Our analysis of the 111 names contained in Table 1 determined none of the names will pose a risk for confusion with Posimir as described in Appendices C through H.

2.2.8 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Anesthesia, Analgesia, and Addiction Products (DAAAP) via e-mail on September 30, 2019. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the Division of Anesthesia, Analgesia, and Addiction Products (DAAAP) on October 3, 2019, they stated no additional concerns with the proposed proprietary name, Posimir.

3 CONCLUSION

The proposed proprietary name, Posimir, is acceptable.

If you have any questions or need clarifications, please contact Davis Mathew, OSE project manager, at 240-402-4559.

3.1 COMMENTS TO DURECT CORPORATION

[d] POCA search conducted on July 16, 2019 in version 4.3.

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

If any of the proposed product characteristics as stated in your submission, received on July 12, 2019, are altered prior to approval of the marketing application, the name must be resubmitted for review.

4 REFERENCES

1. USAN Stems (https://www.ama-assn.org/about/united-states-adopted-names-approved-stems)

USAN Stems List contains all the recognized USAN stems.

2. Phonetic and Orthographic Computer Analysis (POCA)

POCA is a system that FDA designed. As part of the name similarity assessment, POCA is used to evaluate proposed names via a phonetic and orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. Likewise, an orthographic algorithm exists that operates in a similar fashion. POCA is publicly accessible.

Drugs@FDA

Drugs@FDA is an FDA Web site that contains most of the drug products approved in the United States since 1939. The majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present. Drugs@FDA contains official information about FDA-approved *brand name* and *generic drugs*; *therapeutic biological products*, *prescription* and *over-the-counter* human drugs; and *discontinued drugs* (see Drugs @ FDA Glossary of Terms, available at http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm#ther_biological).

RxNorm

RxNorm contains the names of prescription and many OTC drugs available in the United States. RxNorm includes generic and branded:

- Clinical drugs – pharmaceutical products given to (or taken by) a patient with therapeutic or diagnostic intent
- Drug packs – packs that contain multiple drugs, or drugs designed to be administered in a specified sequence

Radiopharmaceuticals, contrast media, food, dietary supplements, and medical devices, such as bandages and crutches, are all out of scope for RxNorm (http://www.nlm.nih.gov/research/umls/rxnorm/overview.html).

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.

APPENDICES

Appendix A

FDA's Proprietary Name Risk Assessment evaluates proposed proprietary names for misbranding and safety concerns.

1. **Misbranding Assessment**: For prescription drug products, OPDP assesses the name for misbranding concerns. For over-the-counter (OTC) drug products, the misbranding assessment of the proposed name is conducted by DNDP. OPDP or DNDP evaluates proposed proprietary names to determine if the name is false or misleading, such as by making misrepresentations with respect to safety or efficacy. For example, a fanciful proprietary name may misbrand a product by suggesting that it has some unique effectiveness or composition when it does not (21 CFR 201.10(c)(3)). OPDP or DNDP provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.
2. **Safety Assessment**: The safety assessment is conducted by DMEPA, and includes the following:

a. Preliminary Assessment: We consider inclusion of USAN stems or other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors (i.e., dosing interval, dosage form/route of administration, medical or product name abbreviations, names that include or suggest the composition of the drug product, etc.) See prescreening checklist below in Table 2*. 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. [e]

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

***Table 2- Prescreening Checklist for Proposed Proprietary Name**

	Answer the questions in the checklist below. Affirmative answers to any of these questions indicate a potential area of concern that should be carefully evaluated as described in this guidance.
Y/N	**Is the proposed name obviously similar in spelling and pronunciation to other names?**
	Proprietary names should not be similar in spelling or pronunciation to proprietary names, established names, or ingredients of other products.
Y/N	**Are there inert or inactive ingredients referenced in the proprietary name?**
	Proprietary names should not incorporate any reference to an inert or inactive ingredient in a way that might create an impression that the ingredient's value is greater than its true functional role in the formulation (21 CFR 201.10(c)(4)).
Y/N	**Does the proprietary name include combinations of active ingredients?**
	Proprietary names of fixed combination drug products should not include or suggest the name of one or more, but not all, of its active ingredients (see 21 CFR 201.6(b)).
Y/N	**Is there a United States Adopted Name (USAN) stem in the proprietary name?**
	Proprietary names should not incorporate a USAN stem in the position that USAN designates for the stem.
Y/N	**Is this proprietary name used for another product that does not share at least one common active ingredient?**
	Drug products that do not contain at least one common active ingredient should not use the same (root) proprietary name.
Y/N	**Is this a proprietary name of a discontinued product?**
	Proprietary names should not use the proprietary name of a discontinued product if that discontinued drug product does not contain the same active ingredients.

b. Phonetic and Orthographic Computer Analysis (POCA): Following the preliminary screening of the proposed proprietary name, DMEPA staff evaluates the proposed name against potentially similar names. In order to identify names with potential similarity to the proposed proprietary name, DMEPA enters the proposed proprietary name in POCA and queries the name against the following drug reference databases, Drugs@fda, CernerRxNorm, and names in the review pipeline using a 55% threshold in POCA. DMEPA reviews the combined orthographic and phonetic matches and group the names into one of the following three categories:

- Highly similar pair: combined match percentage score ≥70%.
- Moderately similar pair: combined match percentage score ≥55% to ≤ 69%.

- Low similarity: combined match percentage score ≤54%.

Using the criteria outlined in the check list (Table 3-5) that corresponds to each of the three categories (highly similar pair, moderately similar pair, and low similarity), DMEPA evaluates the name pairs to determine the acceptability or non-acceptability of a proposed proprietary name. The intent of these checklists is to increase the transparency and predictability of the safety determination of whether a proposed name is vulnerable to confusion from a look-alike or sound-alike perspective. Each bullet below corresponds to the name similarity category cross-references the respective table that addresses criteria that DMEPA uses to determine whether a name presents a safety concern from a look-alike or sound-alike perspective.

- For highly similar names, differences in product characteristics often cannot mitigate the risk of a medication error, including product differences such as strength and dose. Thus, proposed proprietary names that have a combined score of ≥ 70 percent are at risk for a look-alike sound-alike confusion which is an area of concern (See Table 3).
- Moderately similar names are further evaluated to identify the presence of attributes that are known to cause name confusion.
    - Name attributes: We note that the beginning of the drug name plays a significant role in contributing to confusion. Additionally, drug name pairs that start with the same first letter and contain a shared letter string of at least 3 letters in both names are major contributing factor in the confusion of drug names[f]. We evaluate all moderately similar names retrieved from POCA to identify the above attributes. These names are further evaluated to identify overlapping or similar strengths or doses.
    - Product attributes: Moderately similar names of products that have overlapping or similar strengths or doses represent an area for concern for FDA. The dose and strength information is often located in close proximity to the drug name itself on prescriptions and medication orders, and the information can be an important factor that either increases or decreases the potential for confusion between similarly named drug pairs. The ability of other product characteristics to mitigate confusion (e.g., route, frequency, dosage form) may be limited when the strength or dose overlaps. DMEPA reviews such names further, to determine whether sufficient differences exist to prevent confusion. (See Table 4).

- Names with low similarity that have no overlap or similarity in strength and dose are generally acceptable (See Table 5) unless there are data to suggest that the name might be vulnerable to confusion (e.g., prescription simulation study suggests that the name is likely to be misinterpreted as a marketed product). In these instances, we would reassign

[f] Shah, M, Merchant, L, Characteristics That May Help in the Identification of Potentially Confusing Proprietary Drug Names. Therapeutic Innovation & Regulatory Science, September 2016

a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.

c. FDA Prescription Simulation Studies: DMEPA staff also conducts a prescription simulation studies using FDA health care professionals.

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

In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, inpatient medication orders and/or outpatient prescriptions are written, each consisting of a combination of marketed and unapproved drug products, including the proposed name. These orders are optically scanned and one prescription is delivered to a random sample of participating health professionals via e-mail. In addition, a verbal prescription is recorded on voice mail. The voice mail messages are then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants record their interpretations of the orders which are recorded electronically.

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

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

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

When provided, DMEPA considers external proprietary name studies conducted by or for the Applicant/Sponsor and incorporates the findings of these studies into the overall risk assessment.

The DMEPA primary reviewer assigned to evaluate the proposed proprietary name is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name.

Table 3. Highly Similar Name Pair Checklist (i.e., combined Orthographic and Phonetic score is ≥ 70%).

Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may render the names less likely to confusion, provided that the pair does not share a common strength or dose.			
Orthographic Checklist		Phonetic Checklist	
Y/N	Do the names begin with different first letters? *Note that even when names begin with different first letters, certain letters may be confused with each other when scripted.*	**Y/N**	Do the names have different number of syllables?
Y/N	Are the lengths of the names dissimilar* when scripted? **FDA considers the length of names different if the names differ by two or more letters.*	**Y/N**	Do the names have different syllabic stresses?
Y/N	Considering variations in scripting of some letters (such as *z* and *f*), is there a different number or placement of upstroke/downstroke letters present in the names?	**Y/N**	Do the syllables have different phonologic processes, such vowel reduction, assimilation, or deletion?
Y/N	Is there different number or placement of cross-stroke or dotted letters present in the names?	**Y/N**	Across a range of dialects, are the names consistently pronounced differently?
Y/N	Do the infixes of the name appear dissimilar when scripted?		
Y/N	Do the suffixes of the names appear dissimilar when scripted?		

Table 4: Moderately Similar Name Pair Checklist (i.e., combined score is ≥55% to ≤69%).

Step 1	Review the DOSAGE AND ADMINISTRATION and HOW SUPPLIED/STORAGE AND HANDLING sections of the prescribing information (or for OTC drugs refer to the Drug Facts label) to determine if strengths and doses of the name pair overlap or are very similar. Different strengths and doses for products whose names are moderately similar may decrease the risk of confusion between the moderately similar name pairs. Name pairs that have overlapping or similar strengths or doses have a higher potential for confusion and should be evaluated further (see Step 2). Because the strength or dose could be used to express an order or prescription for a particular drug product, overlap in one or both of these components would be reason for further evaluation. For single strength products, also consider circumstances where the strength may not be expressed. For any i.e. drug products comprised of more than one active ingredient, consider whether the strength or dose may be expressed using only one of the components. To determine whether the strengths or doses are similar to your proposed product, consider the following list of factors that may increase confusion: • Alternative expressions of dose: 5 mL may be listed in the prescribing information, but the dose may be expressed in metric weight (e.g., 500 mg) or in non-metric units (e.g., 1 tsp, 1 tablet/capsule). Similarly, a strength or dose of 1000 mg may be expressed, in practice, as 1 g, or vice versa. • Trailing or deleting zeros: 10 mg is similar in appearance to 100 mg which may potentiate confusion between a name pair with moderate similarity. • Similar sounding doses: 15 mg is similar in sound to 50 mg
Step 2	Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may reduce the likelihood of confusion for moderately similar names **with** overlapping or similar strengths or doses.

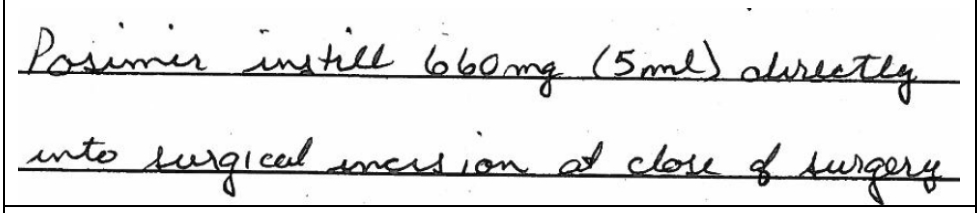
	Orthographic Checklist (Y/N to each question) • Do the names begin with different first letters? Note that even when names begin with different first letters, certain letters may be confused with each other when scripted. • Are the lengths of the names dissimilar* when scripted? *FDA considers the length of names different if the names differ by two or more letters. • Considering variations in scripting of some letters (such as *z* and *f*), is there a different number or placement of upstroke/downstroke letters present in the names? • Is there different number or placement of cross-stroke or dotted letters present in the names? • Do the infixes of the name appear dissimilar when scripted? • Do the suffixes of the names appear dissimilar when scripted?	Phonetic Checklist (Y/N to each question) • Do the names have different number of syllables? • Do the names have different syllabic stresses? • Do the syllables have different phonologic processes, such vowel reduction, assimilation, or deletion? • Across a range of dialects, are the names consistently pronounced differently?

Table 5: Low Similarity Name Pair Checklist (i.e., combined score is ≤54%).

Names with low similarity are generally acceptable unless there are data to suggest that the name might be vulnerable to confusion (e.g., prescription simulation study suggests that the name is likely to be misinterpreted as a marketed product). In these instances, we would reassign a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.

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

Figure 1. Posimir Study (Conducted on July 23, 2019)

Handwritten Medication Order/Prescription	Verbal Prescription
Medication Order:  Outpatient Prescription:  	Posimir Take to clinic. Dispense 1 vial

FDA Prescription Simulation Responses (Aggregate Report)

217 People Received Study
86 People Responded

Study Name: Posimir

Total	18	21	47	
INTERPRETATION	**OUTPATIENT**	**VOICE**	**INPATIENT**	**TOTAL**
POSAMEIRE	0	1	0	1
POSAMERE	0	2	0	2
POSIMER	0	0	2	2
POSIMERE	0	3	0	3
POSIMIE	0	0	2	2
POSIMIR	14	7	41	62
POSIMIRF	0	0	1	1
POSIMIS	0	0	1	1
POSINIR	4	0	0	4
POZAMIR	0	4	0	4
POZIMERE	0	3	0	3
POZMIR	0	1	0	1

Appendix C: Highly Similar Names (e.g., combined POCA score is ≥70%)

No.	**Proposed name:** Posimir **Established name:** bupivacaine **Dosage form:** Extended-Release Solution **Strength(s):** 132 mg/mL **Usual Dose:** 5 mL (660 mg) once per surgical procedure	**POCA Score (%)**	**Orthographic and/or phonetic differences in the names sufficient to prevent confusion** **Other prevention of failure mode expected to minimize the risk of confusion between these two names.**
1.	Posicor	76	Brand discontinued with no generic equivalents available. NDA 020689 withdrawn FR effective 09/17/2001.
2.	Primor	70	Veterinary product.
3.	Primor 120	70	Veterinary product.
4.	Primor 1200	70	Veterinary product.
5.	Primor 240	70	Veterinary product.
6.	Primor 600	70	Veterinary product.

Appendix D: Moderately Similar Names (e.g., combined POCA score is ≥55% to ≤69%) with no overlap or numerical similarity in Strength and/or Dose

No.	Name	POCA Score (%)
1.	(b) (4)***	65
2.	Osmitrol	56
3.	Patiromer	61
4.	Procysbi	58
5.	Profasi	56
6.	Prostigmin	60

Appendix E: Moderately Similar Names (e.g., combined POCA score is ≥55% to ≤69%) with overlap or numerical similarity in Strength and/or Dose

No.	**Proposed name:** Posimir **Established name:** bupivacaine **Dosage form:** Extended-Release Solution **Strength(s):** 132 mg/mL **Usual Dose:** 5 mL (660 mg) once per surgical procedure	**POCA Score (%)**	**Prevention of Failure Mode** **In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names**
1.	Baqsimi***	58	This name pair has sufficient orthographic and phonetic differences.
2.	Optimis7	64	This name pair has sufficient orthographic and phonetic differences.
3.	Oscimin	62	This name pair has sufficient orthographic and phonetic differences.

No.	**Proposed name:** Posimir **Established name:** bupivacaine **Dosage form:** Extended-Release Solution **Strength(s):** 132 mg/mL **Usual Dose:** 5 mL (660 mg) once per surgical procedure	**POCA Score (%)**	**Prevention of Failure Mode** **In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names**
4.	Paser	56	This name pair has sufficient orthographic and phonetic differences.
5.	Paser D/R	58	This name pair has sufficient orthographic and phonetic differences.
6.	Pasmol	58	This name pair has sufficient orthographic and phonetic differences.
7.	Polytar	56	This name pair has sufficient orthographic and phonetic differences.
8.	Poviderm	65	This name pair has sufficient orthographic and phonetic differences.
9.	Prevymis	56	This name pair has sufficient orthographic and phonetic differences.
10.	Primacor	57	This name pair has sufficient orthographic and phonetic differences.
11.	Primsol	56	This name pair has sufficient orthographic and phonetic differences.
12.	Proair	56	This name pair has sufficient orthographic and phonetic differences.
13.	Proscar	59	This name pair has sufficient orthographic and phonetic differences.
14.	Prosom	62	This name pair has sufficient orthographic and phonetic differences.
15.	Prostin VR	62	This name pair has sufficient orthographic and phonetic differences.
16.	Simron	56	This name pair has sufficient orthographic and phonetic differences.
17.	Succimer	65	This name pair has sufficient orthographic and phonetic differences.
18.	Tasmar	60	This name pair has sufficient orthographic and phonetic differences.
19.	Toposar	60	This name pair has sufficient orthographic and phonetic differences.
20.	Tosymra	66	This name pair has sufficient orthographic and phonetic differences.
21.	Tussi-Bid	58	This name pair has sufficient orthographic and phonetic differences.

Appendix F: Low Similarity Names (e.g., combined POCA score is ≤54%)

No.	Name	POCA Score (%)
1.	Buphenyl	42
2.	Dysprosium	48
3.	(b) (4) ***	52
4.	Pro-Symbioflor	52
5.	Romiplostim	46
6.	Simponi	54
7.	Trospium	54
8.	Tussanil	54

Appendix G: Names not likely to be confused or not used in usual practice settings for the reasons described**.**

No.	Name	POCA Score (%)	Failure preventions
1.	Bromspiro	57	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
2.	(b) (4) ***	55	(b) (4)
3.	Depinar	58	Brand discontinued with no generic equivalents available. NDA 011208 withdrawn FR effective 04/04/1990.
4.	Disomer	68	Brand discontinued with no generic equivalents available. NDA 011814 withdrawn FR effective 05/06/1985.
5.	Esimil	60	Brand discontinued with no generic equivalents available. NDA 013553 withdrawn FR effective 06/10/1999.
6.	Liposyn II	57	Brand discontinued with no generic equivalents available. NDAs 018997 (10%) and 018991 (20%) withdrawn FR effective 07/21/2017.
7.	Liposyn II 10%	57	Brand discontinued with no generic equivalents available. NDA 018997 withdrawn FR effective 07/21/2017.
8.	Liposyn II 20%	57	Brand discontinued with no generic equivalents available. NDA 018991 withdrawn FR effective 07/21/2017.
9.	Muscinil	60	International product formerly marketed in the United Kingdom.
10.	Parsidol	56	Brand discontinued with no generic equivalents available. NDA 009078 Application Status API effective 01/01/1900.
11.	Paxidorm	55	International product marketed in Singapore and the United Kingdom.
12.	Pedi-Pro	56	Brand discontinued with no generic equivalents available.

No.	Name	POCA Score (%)	Failure preventions
13.	Pfizer-E	56	Brand discontinued with no generic equivalents available. ANDA 061791 withdrawn FR effective 01/14/1992.
14.	Phiso-Med	59	International product marketed in the United Kingdom.
15.	Plasmin	57	International product marketed in Indonesia and Philippines.
16.	Poloxamer	56	Product is not a drug. It is a nonionic triblock copolymer composed of a central hydrophobic chain of polyoxypropylene (poly(propylene oxide)) flanked by two hydrophilic chains of polyoxyethylene (poly(ethylene oxide)).
17.	Poloxamer 124	56	Product is not a drug. It is a surfactant and emulsifying agent. It belongs to a group of compounds known as poloxamers that are made up of three polymer blocks. In cosmetic and personal care product formulations, it functions as a surfactant - emulsifying agent and surfactant - solubilizing agent. It can be used in soaps and cleansers.
18.	Poloxamer 181	56	Product is not a drug. It is a surfactant.
19.	Poloxamer 182	56	Product is not a drug. It is a nonionic triblock copolymer composed of a central hydrophobic chain of polyoxypropylene flanked by two hydrophilic chains of polyoxyethylene. It belongs to a group of compounds known as poloxamers that are made up of three polymer blocks. In cosmetic and personal care product formulations, it functions as a surfactant - cleansing agent. It can be used in soaps and cleansers. It is partially soluble in water.
20.	Poloxamer 184	56	Product is not a drug. It is a nonionic triblock copolymer composed of a central hydrophobic chain of polyoxypropylene flanked by two hydrophilic chains of polyoxyethylene. It belongs to a group of compounds known as poloxamers that are made up of three polymer blocks. In cosmetic and personal care product formulations, it functions as a surfactant - cleansing agent and surfactant - solubilizing agent. It can be used in hair care products and cleansers. It is soluble in water.
21.	Poloxamer 188	56	Product is not a drug. It is a copolymer of polyoxyethylene and polyoxypropylene used for drug delivery as formulation excipients.
22.	Poloxamer 234	56	Product is not a drug. It is a surfactant.
23.	Poloxamer 237	56	Product is not a drug. It is a surfactant.
24.	Poloxamer 331	56	Product is not a drug. It is a nonionic triblock copolymer. It is made up of a main hydrophobic chain of polyoxypropylene bordered on each side by two hydrophilic chains of polyoxyethylene. It is a surfactant.

No.	Name	POCA Score (%)	Failure preventions
25.	Poloxamer 335	56	Product is not a drug. It is polyoxyethylene, polyoxypropylene block polymer used as a surfactant.
26.	Poloxamer 338	56	Product is not a drug. It is a surfactant.
27.	Poloxamer 403	56	Product is not a drug. It is a surfactant.
28.	Poloxamer 407	56	Product is not a drug. It is a hydrophilic non-ionic surfactant of the more general class of copolymers known as poloxamers. Poloxamer 407 is a triblock copolymer consisting of a central hydrophobic block of polypropylene glycol flanked by two hydrophilic blocks of polyethylene glycol (PEG).
29.	Poly D SR	56	Brand discontinued with no generic equivalents available.
30.	Pondimin	60	Product withdrawn from the market due to safety concerns. Additional details available at: https://www.federalregister.gov/documents/2015/09/29/2015-24619/determination-that-pondimin-fenfluramine-hydrochloride-tablets-20-milligrams-and-60-milligrams-and
31.	Postmi	69	International product formerly marketed in the United Kingdom.
32.	Pramimil	57	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
33.	Pressair***	62	Product is not a drug. It is an inhaler device included in the proprietary names of the approved products Duaklir Pressair (NDA 210595) and Tudorza Pressair (NDA 202450).
34.	Pressimmune	56	International product formerly marketed in the United Kingdom.
35.	Profen II	59	Name identified in RxNorm database. Product is deactivated and no generic equivalents are available.
36.	Prominol	56	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
37.	Promit	56	Name identified in RxNorm database. Product is deactivated and no generic equivalents are available.
38.	Prosaid	58	International product formerly marketed in the United Kingdom.
39.	Protium I.V	62	International product marketed in Ireland and the United Kingdom.
40.	Simcor	62	Brand discontinued with no generic equivalents available. NDA 022078 withdrawn FR effective 04/18/2016.
41.	Tusso ZMR	60	Name identified in RxNorm database. Product is deactivated and no generic equivalents are available.

Appendix H: Names not likely to be confused due to absence of attributes that are known to cause name confusion[g].

No.	Name	POCA Score (%)
1.	Calcimar	55
2.	Carospir	58
3.	Combivir	56
4.	Cosamin	62
5.	Diosmin	57
6.	Domitor	58
7.	(b) (4) ***	56
8.	Epivir	56
9.	Fiormor	56
10.	Foscavir	60
11.	(b) (4) ***	56
12.	Midamor	59
13.	(b) (4) ***	56
14.	Opsumit	60
15.	Optimark	60
16.	Optimark	60
17.	Optimyd	55
18.	Optivar	56
19.	Otimar	66
20.	Sensipar	55
21.	Silenor	56
22.	Stimlor	64
23.	(b) (4) ***	56
24.	Swim Ear	58
25.	Testomar	56
26.	Topilar	56
27.	Vospire	60
28.	Vospire ER	56
29.	Yohimar	56

[g] Shah, M, Merchant, L, Chan, I, and Taylor, K. Characteristics That May Help in the Identification of Potentially Confusing Proprietary Drug Names. Therapeutic Innovation & Regulatory Science, September 2016

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

DEBORAH E MYERS
10/04/2019 09:03:18 AM

IRENE Z CHAN on behalf of OTTO L TOWNSEND
10/04/2019 09:12:54 AM

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

Proprietary Name Review

Date:	July 22, 2013
Reviewer:	Vicky Borders-Hemphill, Pharm.D. Division of Medication Error Prevention and Analysis
Team Leader:	Jamie Wilkins Parker, Pharm.D. Division of Medication Error prevention and Analysis
Division Director:	Carol Holquist, RPh. Division of Medication Error Prevention and Analysis
Drug Name and Strength:	Posimir (bupivacaine extended-release solution for instillation) 132 mg/mL (660 mg per 5 mL)
Application Type/Number:	NDA 204803
Applicant/Sponsor:	Durect Corporation
OSE RCM #:	2013-1001

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

CONTENTS

1 INTRODUCTION

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

1.1 REGULATORY HISTORY

On April 12, 2013, Durect Corporation submitted a 505 (b)(2) NDA 204803 for Posimir (bupivacaine extended-release solution for instillation) as a long acting local anesthetic for extended relief of post-surgical pain.

1.2 PRODUCT INFORMATION

The following product information is provided in the April 25, 2013, proprietary name submission.

- Active Ingredient: bupivacaine
- Indication of Use: Post-surgical analgesia
- Route of Administration: Instilled into the surgical incision
- Dosage Form: Sterile solution for instillation
- Strength: 132 mg/mL Bupivacaine (660 mg per 5 mL)
- Dose and Frequency: 5 mL bupivacaine solution intended as single-dose for instillation directly into the surgical incision (b) (4)
- How Supplied: 5 mL single dose vial, 13.2%, 660 mg/5 mL (132 mg/mL) packaged in a 10-unit carton
- Storage: 20º C to 25º C (68º F to 77º F). Protect vial from light and retain in cartoon until time of use.
- Container and Closure Systems: single dose vial
- RLD: Marcaine (bupivacaine hydrochloride) injection (NDA 016964)

2 RESULTS

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

2.1 PROMOTIONAL ASSESSMENT

The Office of Prescription Drug Promotion OPDP determined the proposed name is acceptable from a promotional perspective. DMEPA and the Division of Anesthesia, Analgesia, and Addiction Products (DAAAP) concurred with the findings of OPDP's promotional assessment of the proposed name.

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) SEARCH

The July 1, 2013 search of the United States Adopted Name (USAN) stems did not identify that a USAN stem is present in the proposed proprietary name.

2.2.2 Components of the Proposed Proprietary Name

The Applicant indicated in their submission that the proposed name, Posimir, has no derivation or intended meaning. This proprietary name is comprised of a single word that has medical abbreviations "IM" and "PO" in the name. However, the placement of these letters in the name should minimize any risk of confusion with these medical abbreviations.

2.2.4 FDA Name Simulation Studies

Seventy-nine practitioners participated in DMEPA's prescription studies. The interpretations did not overlap with any currently marketed products nor did the misinterpretations sound or look similar to any currently marketed products or any products in the pipeline. Thirty-six of the participants interpreted the name correctly as "Posimir", with correct interpretations occurring in the inpatient and outpatient written studies and voice prescription. DMEPA considered various misinterpretations in our look-alike and sound-alike searches and analysis (see Appendix B). See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

2.2.5 Comments from Other Review Disciplines at Initial Review

In response to the OSE, June 17, 2013 e-mail, DAAAP did not forward any comments or concerns relating to the proposed proprietary name at the initial phase of the review.

2.2.6 Failure Mode and Effects Analysis of Similar Names

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

Table 1: Collective List of Potentially Similar Names (DMEPA, EPD, Other Disciplines, and FDA)					
Look Similar					
Name	***Source***	***Name***	***Source***	***Name***	***Source***
Darunavir	FDA	Pasimar	FDA	Posinol	FDA
Detemir Insulin	FDA	Pasiona	FDA	Poslam	FDA
Dormin	FDA	Pasmol	FDA	Premarin	FDA
Fosamax	FDA	Perazine	FDA	Remeron	FDA
Pamelor	FDA	Perimax Perio Rinse	FDA	Resinol	FDA
Paser	FDA	Perisine	FDA	Rozerem	FDA
		Posinist	FDA	Tremin	FDA
Look and Sound Similar					
Name	***Source***	***Name***	***Source***	***Name***	***Source***
Porfimer	FDA	Tasmar	FDA	Posimir	FDA

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

2.2.7 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to DAAAP via e-mail on June 17, 2013. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from DAAAP on June 28, 2013, they stated no additional concerns with the proposed proprietary name, Posimir.

3 CONCLUSIONS

The proposed proprietary name is acceptable from both a promotional and safety perspective. If you have further questions or need clarifications, please contact Vaishali Jarral, project manager, at 301-796-4248.

3.1 COMMENTS TO THE APPLICANT

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

The proposed proprietary name must be re-reviewed 90 days prior to approval of the NDA. The results are subject to change. If any of the proposed product characteristics as stated in your April 25, 2013, submission are altered, the name must be resubmitted for review.

4 REFERENCES

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

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

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

   POCA is a database which was created for the Division of Medication Error Prevention and Analysis, FDA. As part of the name similarity assessment, proposed names are evaluated via a phonetic/orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. Likewise, an orthographic algorithm exists which operates in a similar fashion.

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

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

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

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

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

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

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

   Drugs@FDA contains most of the drug products approved since 1939. The majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present. Drugs@FDA contains official information about FDA approved brand name, generic drugs, therapeutic biological products, prescription and over-the-counter human drugs and discontinued drugs and "Chemical Type 6" approvals.

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

   USPTO provides information regarding patent and trademarks.

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

   Clinical Pharmacology contains full monographs for the most common drugs in clinical use, plus mini monographs covering investigational, less common, combination, nutraceutical and nutritional products. It also provides a keyword search engine.

9. ***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.

10. ***Access Medicine (www.accessmedicine.com)***

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

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

    USAN Stems List contains all the recognized USAN stems.

12. ***Red Book (www.thomsonhc.com/home/dispatch)***

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

13. ***Lexi-Comp (www.lexi.com)***

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

14. ***Medical Abbreviations (www.medilexicon.com)***

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

15. ***CVS/Pharmacy (www.CVS.com)***

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

16. ***Walgreens (www.walgreens.com)***

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

17. ***Rx List (www.rxlist.com)***

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

18. ***Dogpile (www.dogpile.com)***

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

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

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

APPENDICES

Appendix A

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

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

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

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

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

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

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

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

The DMEPA considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA compares the proposed proprietary name with the proprietary and established name of existing and proposed drug products and names currently under review at the FDA. DMEPA compares the pronunciation of the proposed proprietary name with the pronunciation of other drug names because verbal communication of medication names is common in clinical settings. DMEPA examines the phonetic similarity using patterns of speech. If provided, DMEPA will consider the Sponsor's intended pronunciation of the proprietary name. However, DMEPA also considers a variety of pronunciations that could occur in the English language because the Sponsor has little control over how the name will be spoken in clinical practice. The orthographic appearance of the proposed name is evaluated using a number of different handwriting samples. DMEPA applies expertise gained from root-cause analysis of postmarketing medication errors to identify sources of ambiguity within the name that could be introduced when scripting (e.g.,"T" may look like "F," lower case 'a' looks like a lower case 'u,' etc). Additionally, other orthographic attributes that determine the overall appearance of the drug name when scripted (see Table 1 below for details).

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

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

Type of Similarity	**Considerations when Searching the Databases**		
	Potential Causes of Drug Name Similarity	*Attributes Examined to Identify Similar Drug Names*	*Potential Effects*
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	• Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication • Names may look similar when scripted and lead to drug name confusion in written communication
	Orthographic similarity	Similar spelling Length of the name/Similar shape Upstrokes Down strokes Cross-strokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	• Names may look similar when scripted, and lead to drug name confusion in written communication
Sound-alike	Phonetic similarity	Identical prefix Identical infix Identical suffix Number of syllables Stresses Placement of vowel sounds Placement of consonant sounds Overlapping product characteristics	• Names may sound similar when pronounced and lead to drug name confusion in verbal communication

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

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

1. Database and Information Sources

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

2. Expert Panel Discussion

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

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

3. FDA Prescription Simulation Studies

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

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

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

4. Comments from Other Review Disciplines

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

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

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

5. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

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

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

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

characteristics listed in Section 1.2 of this review. The Safety Evaluator then analyzes the proposed proprietary name in the context of the usual practice setting and works to identify potential failure modes and the effects associated with the failure modes.

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

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

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

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

> ***"Could the confusion of the drug names conceivably result in medication errors in the usual practice setting?"***

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

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

a. OPDP finds the proposed proprietary name misleading from a promotional perspective, and the Review Division concurs with OPDP's findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a PROPRIETARY name or otherwise [21 U.S.C 321(n); See also 21 U.S.C. 352(a) & (n)].

b. DMEPA identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].

c. FMEA identifies the potential for confusion between the proposed proprietary name and other proprietary or established drug name(s), and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.

d. The proposed proprietary name contains an USAN (United States Adopted Names) stem.

e. DMEPA identifies a potential source of medication error within the proposed proprietary name. For example, the proprietary name may be misleading or, inadvertently, introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug and another drug product but involve a naming characteristic that when incorporated into a proprietary name, may be confusing, misleading, cause or contribute to medication errors.

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

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

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

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

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

Appendix B: Letters and Letter Strings with Possible Orthographic or Phonetic Misinterpretation

Letters in Name Posimir	**Scripted May Appear as**	**Spoken May Be Interpreted as**
Capital 'P'	D, R, S, F	B, F, Ph, T
Lower case 'p'	g, j, l, q, f	B, f, ph, t
Lower case 'o"	a, c, e ,u	oh
Lower case 's'	g, n, r	x, z, v
Lower case 'i'	e, l	y
Lower case 'm'	rn, nn, n, v, w, z	n
Lower case 'i'	e, l	y
Lower case 'r'	s, n, v	
Letter strings in Name Posimir	**Scripted May Appear as**	**Spoken May Be Interpreted as**
Pos-	Pas, Pes, Poi	Fos, Hav, Pav, Paz, Poz, Prov, Tos
-imir	mie, mii, mu, mer, mic, mil, mire	neer, nir, ner, near, mere,
Si	x	
ir	U, n	

Appendix C: Prescription Simulation Samples and Results

Figure 1. Posimir Study (Conducted on May 3, 2013)

Handwritten Requisition Medication Order	Verbal Prescription
Medication Order: Posimir 5 mL instilled in surgical incision	"Posimir, bring to clinic, dispense 10 ml"
Outpatient Prescription: Posimir 10ML to clinic	

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

191 People Received Study
79 People Responded

Total	30	20	29	
INTERPRETATION	OUTPATIENT	VOICE	INPATIENT	TOTAL
PONINIR	0	0	1	1
POSAMERE	0	2	0	2
POSAMIR	0	3	0	3
POSIMAR	1	0	0	1
POSIMEER	0	1	0	1
POSIMEIR	0	1	0	1
POSIMER	6	0	0	6
POSIMERE	0	2	0	2
POSIMIN	0	0	1	1
POSIMIR	13	5	18	36
POSIMIRLOML	1	0	0	1
POSIMIS	0	0	7	7
POSIMO	1	0	0	1
POSIMOR	4	0	0	4
POSIMOR10ML	1	0	0	1
POSIMOX	1	0	0	1
POSIMUR	1	0	0	1
POSINIER	1	0	0	1
POSINIS	0	0	1	1
POSIRI	0	0	1	1
POSOMERE	0	1	0	1
POSSAMER	0	1	0	1
POSSAMERE	0	2	0	2
POSSIMERE	0	1	0	1
POSSIMIR	0	1	0	1

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

No.	Proprietary Name	Active Ingredient	Similarity to Posimir	Failure preventions
1	Detemir Insulin	active ingredient in Levemir	Orthographic	The pair have sufficient orthographic differences
2	Pamelor	nortriptyline	Orthographic	The pair have sufficient orthographic differences
4	Pasimar		Orthographic	Name identified in Saegis. Unable to find product characteristics in commonly used drug databases
5	Pasiona		Orthographic	Name identified in USPTO. Unable to find product characteristics in commonly used drug databases
6	Pasmol	ethaverine HCl	Orthographic	The pair have sufficient orthographic differences
7	Perazine	active ingredient; phenothiazine psychotropic	Orthographic	Foreign name- only marketed in Germany, Poland, Yugoslavia and the Netherlands
8	Posimir	bupivacaine	Orthographic and Phonetic	Current name under review
9	Posinist		Orthographic	The pair have sufficient orthographic differences.
10	Posinol		Orthographic	The pair have sufficient orthographic differences.
11	Premarin	estrogens, conjugated	Orthographic	The pair have sufficient orthographic differences
12	Remeron	mirtazapine	Orthographic	The pair have sufficient orthographic differences
13	Resinol	calamine/resorcinol/zinc oxide	Orthographic	The pair have sufficient orthographic differences
14	Tremin	Trihexyphenidyl hydrochloride	Orthographic	Product withdrawn FR effective 12/10/1992. Generics are available

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

Posimir (bupivacaine) **Strength:** 13.2%, 660 mg/5 mL (132 mg/mL) **Dosage form:** solution for instillation **Dose:** 5 mL **Frequency:** once **Route of Administration:** instillation into surgical wound during surgery **Supplied:** 5 mL single dose vial, packaged in a 10-unit carton	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	Prevention of Failure Mode In the conditions outlined below, the following combination of factors are expected to minimize the risk of confusion between these two names
Darunavir (active ingredient in Prezista; no generic equivalents available) **Strength:** 75 mg, 150 mg, 400 mg, 600 mg, 800 mg and 100 mg/mL **Dosage form:** tablet and suspension **Dose:** 800 mg (one 800 mg tablet or two 400 mg tablets) taken with ritonavir 100 mg once daily, 600 mg (one 600 mg tablet) taken with ritonavir 100 mg twice daily **Route of Administration:** oral	Orthographic similarity: Both names contain letters that may be similarly scripted in the prefix “Posi” vs. “Daru”. The suffix “mir” in Posimir is may appear similar to the suffix “vir” when scripted. Overlapping product characteristics: none	Orthographic differences: The infix ”na” in Darunavir elongates the name Product characteristic differences: **Frequency:** Posimir one time administration vs. Darunavir once daily or twice daily **Strength:** Posimir has a single strength which may be omitted from a prescription vs. Darunavir has several strengths and will be required on the prescription

Posimir (bupivacaine) **Strength:** 13.2%, 660 mg/5 mL (132 mg/mL) **Dosage form:** solution for instillation **Dose:** 5 mL **Frequency:** once **Route of Administration:** instillation into surgical wound during surgery **Supplied:** 5 mL single dose vial, packaged in a 10-unit carton	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	Prevention of Failure Mode In the conditions outlined below, the following combination of factors are expected to minimize the risk of confusion between these two names
Dormin (diphenhydramine) **Strength:** 25 mg **Dosage form:** capsule **Dose:** 25 to 50 mg every 4 to 6 hours or 50 mg at bedtime **Route of Administration:** oral	Orthographic similarity: Both names contain letters that may be similarly scripted in the prefix "Pos" vs. "Dor", and the suffix "mir" vs. "min" may appear orthographically similar when scripted. The names have similar shape and length. Overlapping product characteristics: **Route:** Both product have a single strength which may be omitted from the prescription	Product characteristic differences: **Frequency:** Posimir one time administration vs. Dormin every 4 to 6 hours or at bedtime
Fosamax (alendronate) **Strength:** 5 mg, 10 mg, 40 mg, 35 mg, 70 mg **Dosage form:** tablet and oral solution **Dose:** 5 mg once daily, 10 mg once daily, 70 mg once weekly, 35 mg once weekly, 40 mg once daily **Route of Administration**: oral	Orthographic similarity: Both names contain letters throughout that may appear similar when scripted. Both names have a similar shape and length. Overlapping product characteristics: Dose: 5 mg vs. 5 mL	Product characteristic differences: **Strength:** Posimir has a single strength which may be omitted from a prescription vs. Fosamax has several strengths and will be required on the prescription **Frequency:** Posimir one time administration vs. Fosamax once daily or once weekly

Posimir (bupivacaine) **Strength:** 13.2%, 660 mg/5 mL (132 mg/mL) **Dosage form:** solution for instillation **Dose:** 5 mL **Frequency:** once **Route of Administration:** instillation into surgical wound during surgery **Supplied:** 5 mL single dose vial, packaged in a 10-unit carton	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	Prevention of Failure Mode In the conditions outlined below, the following combination of factors are expected to minimize the risk of confusion between these two names
Perimax Perio Rinse (hydrogen peroxide) **Strength:** 1.5% (240 mL bottle) **Dosage form:** solution **Dose:** swish and spit up a capful up to four times daily **Route of Administration**: oral	Orthographic similarity: Both names contain letters throughout that may appear similar when scripted. The names have similar shape and length. Overlapping product characteristics: **Dosage form:** solution	Product characteristic differences: **Frequency:** Posimir one time administration vs. Perimax up to four times daily **Dose:** Posimir 5 mL vs. Perimax uses the cap for dosing
Perisine (acetaminophen phenyltoloxamine citrate) **Strength:** 325 mg/ 30 mg (OTC) **Dosage form:** tablet **Dose:** 1 tablet every 4-6 hours **Route of Administration:** oral	Orthographic similarity: Both names contain letters in the prefix that may appear similar when scripted “Posi” vs. “Peri”, and the suffix “mir” vs. “sin” The names have similar shape. Overlapping product characteristics: **Strength:** single strength may be omitted from the prescription	Orthographic differences: The suffix “sine” in perisine elongates the name Product characteristic differences: **Frequency:** Posimir one time administration vs. Perisine every 4 to 6 hours

Posimir (bupivacaine) **Strength:** 13.2%, 660 mg/5 mL (132 mg/mL) **Dosage form:** solution for instillation **Dose:** 5 mL **Frequency:** once **Route of Administration:** instillation into surgical wound during surgery **Supplied:** 5 mL single dose vial, packaged in a 10-unit carton	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	Prevention of Failure Mode In the conditions outlined below, the following combination of factors are expected to minimize the risk of confusion between these two names
Rozerem (ramelteon) **Strength:** 8 mg **Dosage form:** tablet **Dose:** Insomnia: 8 mg taken within 30 min of bedtime **Route of Administration:** oral	Orthographic similarity: Both names contain letters that may be similarly scripted in the prefix "Po" vs. "Ro. The names have similar shape when the letter "z" in Rozerem is not scripted with a downstroke. Overlapping product characteristics: **Strength:** single strength may be omitted from the prescription	Orthographic differences: The letter strings in the infix and suffix "simir" in Posimir is not orthographically similar to "zerem" in Rozerem Product characteristic differences: **Frequency:** Posimir one time administration vs. Rozerem at bedtime

Posimir (bupivacaine) **Strength:** 13.2%, 660 mg/5 mL (132 mg/mL) **Dosage form:** solution for instillation **Dose:** 5 mL **Frequency:** once **Route of Administration:** instillation into surgical wound during surgery **Supplied:** 5 mL single dose vial, packaged in a 10-unit carton	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	Prevention of Failure Mode In the conditions outlined below, the following combination of factors are expected to minimize the risk of confusion between these two names
Tasmar (tolcapone) **Strengths:** 100 mg and 200 mg **Dosage form:** tablets **Dose:** initial dose is always 100 mg three times daily. The recommended daily dose is 100 mg three times daily. Only prescribed for patients taking concomitant carbidopa levodopa therapy **Route of Administration:** oral	Orthographic similarity: Both names contain letters in the prefix that may appear similar when scripted "Pos" vs. "Tas" and contains letters in the suffix that may appear similar when scripted "mir" vs. "mar". Phonetic similarity: Both names begin with prefixes that may sound similar "Pos" vs. "Tas" and end with suffixes that may sound similar "mir" vs. "mar" Overlapping product characteristics: None	Phonetic differences: Posimir prefix contains the letter "o" which may be pronounced using the short "o" sound vs. Tasmar prefix contains the letter "a" which may be pronounced using the short "a" sound and Posimir suffix "mir" may be pronounced using the short "i" sound vs. Tasmar suffix "mar" may be pronounced using the sound "uh" for the letter "a". Product characteristic differences: **Frequency:** Posimir one time administration vs. Tasmar three times daily **Strength:** Posimir single strength may be omitted vs. Tasmar has multiple strengths and must be stated on the prescription

Posimir (bupivacaine) **Strength:** 13.2%, 660 mg/5 mL (132 mg/mL) **Dosage form:** solution for instillation **Dose:** 5 mL **Frequency:** once **Route of Administration:** instillation into surgical wound during surgery **Supplied:** 5 mL single dose vial, packaged in a 10-unit carton	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)	Prevention of Failure Mode In the conditions outlined below, the following combination of factors are expected to minimize the risk of confusion between these two names
Paser (aminosalicyclic acid) **Strength:** 4 gram **Dosage form:** delayed release granules in packet **Dose:** Crohn's disease, Remission maintenance: 500 mg three times daily or Tuberculosis: 4 grams three times daily **Route of Administration:** oral	Orthographic similarity: Both names contain letters in the prefix that may appear similar when scripted "Pos" vs. "Pas" and contain letters in the suffix that may appear similar when scripted "ir" vs. "er". Phonetic similarity: Both names begin with prefixes that may sound similar "Pos" vs. "Pas" and end with suffixes that may sound similar "ir" vs. "er" Overlapping product characteristics: None	Orthographic differences: The letters in Posimir suffix "imir" are not similar and are more elongated compared to the letters in suffix of Paser "er" when scripted. Product characteristic differences: **Frequency:** Posimir one time administration vs. Paser three times daily **Dose:** Posimir dose may be omitted vs. Paser dose must be stated on the prescription as one packet or 4 grams
Poslam (salicyclic acid) **Strength:** 2% **Dosage form:** ointment in 45 gram tube **Dose:** Use as directed **Route of Administration:** topical	Orthographic similarity: Both names contain letters in the prefix that may appear similar when scripted "Posi" vs. "Posl" Overlapping product characteristics: **Dose:** dose may be omitted	Orthographic differences: The letters in Posimir suffix "mir" are not similar and are more elongated compared to the letters in suffix of Poslam "am" when scripted. Product characteristic differences: **Frequency:** Posimir one time administration vs. Poslam use as directed

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This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

BRENDA V BORDERS-HEMPHILL
07/22/2013

CAROL A HOLQUIST on behalf of JAMIE C WILKINS PARKER
07/22/2013
Signing on behalf of Jamie Wilkins Parker

CAROL A HOLQUIST
07/22/2013